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Case of pellagra, showing typic "gauntlet." (Patient of Dr. G. A. Zeller.)

PELLAGRA

AN AMERICAN PROBLEM

BY

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SECOND EDITION

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no. 1.

TO
CHARLES E. BOYNTON, A. B., M. D.,
THIS VOLUME IS INSCRIBED
AS A TRIBUTE TO HIS HIGH PROFESSIONAL
ATTAINMENTS AND IN REMEMBRANCE
OF HIS MANY ACTS OF KINDNESS,
BY THE AUTHOR

PREFACE TO THE SECOND EDITION

THE success of the first edition of this book seemed to indicate that it filled a need of the profession. In this second edition many changes and additions have been made, bringing the consideration of Pellagra as a national problem up to our present state of knowledge.

The chapter on Etiology contains the result of the investigations of Dr. Joseph Goldberger, Special U. S. Agent for the study of this disease, and the Thompson-McFadden Pellagra Commission, whose careful and scientific labors have received deserved commendation. The efforts of other students have also been recognized.

The chapter on Treatment contains a number of late therapeutic suggestions, including the employment of emetin for the frequently ameba-infected mouth and intestines, the scarlet ointment for obstinate dermatitis, and others, which I have found helpful.

I am indebted to numerous friends for criticisms and constructive advice; and especially to the members of the Thompson-McFadden Commission, who have both officially and personally extended valuable aid, is offered grateful acknowledgment.

While the causation of Pellagra is not yet entirely proved, the conviction is expressed that we are much nearer the goal of etiologic certainty, pathologic assurance, and consequent therapeutic confidence.

GEORGE M. NILES.

920 CANDLER BUILDING,
ATLANTA, GA.

January, 1916.

PREFACE

IN presenting this work I feel that a literature on the subject of pellagra should be advanced by American observers.

We should not be deterred because of its recent visitation, nor should we be content to leave its investigation to our friends in Europe, though they have been wrestling with this problem for near two centuries; and we may find it difficult to rival them in erudition as well as the profundity with which they have considered some of the unsolved pathologic and etiologic questions. A condition confronts us, and we must needs be up and doing in order to meet it.

I have no apology to offer for expressing my candid opinions and firm convictions. Should subsequent experience and knowledge convince me that I have fostered error, I shall be the first to announce it and make the necessary amends. No advancement has ever been made except by following a new idea to an established fact, and in the light which is now guiding me I can see no incorrect premise nor any false conclusions; yet I do not expect the approbation of all whose opinions I court and whose words I respect.

To go forward and not backward in the management of this threatened scourge will require much clinical observation, much laboratory labor, special technic in the examination and treatment of the various phases of pellagra, a

practical knowledge of physiology and physiologic chemistry, the medical uses of special drugs, baths, waters, and electricity, and, with it all, time and patience.

It will be most interesting a few years hence to look back in a retrospective manner on the efforts of to-day, on the possibly erroneous viewpoints with which we have considered pellagra, and our somewhat halting footsteps in its therapeutics. We are glad in this connection, however, to lay to our souls the flattering unction that our efforts are at least sincere and justified by present results.

To many kind friends I convey my appreciation for helpful suggestions and other courtesies; but particularly do I wish to thank Dr. J. W. Babcock, of Columbia, and Dr. C. H. Lavinder, of the Public Health and Marine-Hospital Service, for both their encouragement and consideration.

To the medical profession I offer this book for what it is, not claiming that it speaks the "last word," but that it represents the labors of a student who is endeavoring with a spirit of courage and optimism to contribute a worthy portion to the sum total of our information concerning pellagra, this American problem.

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PELLAGRA

CHAPTER I

GENERAL CONSIDERATIONS, HISTORIC AND OTHERWISE

PELLAGRA, as an American problem, is now receiving marked attention in many sections of this country. Up to less than eight years ago it appeared upon the sociologic horizon as a cloud no larger than a man's hand, but it has continued to grow and expand, until at present it looms up before the sober observer with portentous solemnity.

Pellagra may be defined as an endemic malady, characterized by an erythema (generally symmetric) upon the exposed surfaces of the body, by gastro-intestinal disturbances, and by nervous and psychic phenomena.

This definition is necessarily incomplete, for to describe this protean disease in a few words would require the graphic imagination of a Carlyle, or the word-painting of a Macaulay.

The synonyms for pellagra are numerous, among which are Alpine Scurvy, Asturian Leprosy, Asturian Rose, Disease of the Landes, Maidismus, Psychoneurosis Maidica,

Mal de la Rosa, Mal del Sole, Mal de Misere, Mal del Padrone, and many others.

To Frapolli we owe the present name of the disease (*pelle*, skin, and *agra*, rough), and the same writer declared that the disease was an ancient one, and none other than the sickness *pellarella*, which was noted in 1578 by the authorities of the Hospital Major, of Milan.

As to the pronunciation, the varieties are almost legion. It would seem fair to permit a man the privilege of pronouncing his own name; or to the resident of a state or country the like privilege of pronouncing the name of his abode. For instance, we grant to the residents of Iowa the right to say *Ioway*, or to those living in Arkansas the rather bizarre-sounding *Arkansaw*. By this same token it seems proper to permit the Italians, who gave us the name, to also teach us the pronunciation. After consulting with not a few, but with many educated Italians, those in a position to speak with authority, the writer is convinced that the most widely accepted pronunciation gives the *a* in pellagra the same sound as in the word *father*, with the accent on the second syllable.

Some, of course, will take issue with this, as would be the case with any other word not possessing the sanction of ancient and world-wide custom in its pronunciation; but the sound of *a* in this word, as given above, is probably used more than any other.

To trace back the history of this disease, among the rather scattered archives of the middle ages, is both interesting and difficult. Dr. Howard D. King, of New Orleans, recently contributed a most valuable historic study

of pellagra, and to him, as well as to Dr. A. Marie, we are indebted for much of this data.

To weave a history of pellagra without encountering the visage of maize seems almost impossible. Through the tangled skein, as it is interwoven with the destinies of several nations and peoples, we see the rise and decline of pellagra almost coincident with the consumption of Indian corn; and, try as we may, we cannot disassociate the two.

In 1600 Baruino, in a medical treatise, called attention to a peculiar malady prevailing among certain tribes of the American Indians. From his incomplete description, it apparently resembled the pellagra of to-day. Even then he ascribed it to the use of corn, which the Indians used constantly as a part of their diet.

Francisco Scipione, an Italian poet, archeologist, and litterateur, also described a similar disease but a few months after Baruino, his description being much more complete. About this time there was also noted a peculiar disease among horses, in which those animals seemed both paretic and tabetic, showing a malnutrition with loss of hair. This was supposed to have been produced by feeding them spoiled corn.

In Spain corn was introduced as an article of food in the period between 1680 and 1700. Strange to say, the first authentic accounts of pellagra appeared just about this time. According to Babes and Sion, as claimed by Dr. Babcock, it is probable that pellagra appeared in Europe long before its scientific description, but was classed as either gastro-intestinal, or nervous, or mental, or leprous, or scorbutic diseases. It is, therefore, some-

what difficult to determine whether or not pellagra appeared in Europe before the advent of Indian corn as a food.

The first really scientific account is ascribed to Gaspar Casal, who, in 1735, observed it in the vicinity of Oviedo. Several years later he wrote of it fully, describing it as seen in the Asturias, and giving it the name "Mal de Rosa." For a long time the disease was found only in this region, and in somewhat narrow limits. Even to this day Oviedo seems a focus.

In Italy it appeared about twenty-five years later than in Spain. Frapolli, to whom, as previously said, we are indebted for the word pellagra, believed he had found a picture of pellagra in the description of *la pellarella* in 1578. This was more probably a case of syphilis. About the time Frapolli named it, Adoardi, of Venetia, called it "scorbutus alpinus."

By 1776, also a notable year in American annals, the disease had spread to such an extent that the Venetian authorities, at the request of the Sanitary Commission of Venice, issued an edict prohibiting the sale or exchange in the public markets of corn having a bad odor or taste, or which was discolored. Even at that time, exacerbations and remissions of pellagra during different seasons of the year were noted, for D'Oleggio, in 1784, suggested the term "vernal insolation," meaning the "sunburn of spring." Also in that year a special hospital for those afflicted in this manner, and for special study of the disease, was established in Legano by royal warrant, and called the Joseph II Pellagra Asylum. The elder Strambio, a man admirably fitted by both education and tem-

perament for such a position, was appointed chief physician.

From this period, up to 1839, but little was done to check the ravages of pellagra, when Ballardino declared that it was produced by eating damaged maize, claiming that he had demonstrated it beyond a peradventure. His views, as happens to any one making radical statements, met with ridicule, and, while the discussion waxed warm, the flames of the disease spread with amazing rapidity. From 1839 to 1856, a space of seventeen years, there was an increase of from 14 to 28 per thousand, or from 20,282 to 38,777. This alarming increase brought the Lombard government to action, and it was high time. A commission from the Institute Lombardo was appointed to investigate, and to report ways and means to combat this state of affairs. Commissions, like petit juries, are often remarkable bodies, and this was no exception. They reported that while, in their opinion, Ballardino's theory as to spoiled or damaged maize being a causative factor was in the main correct, they did not believe that a diet free from maize would either exert a favorable influence or prevent the disease.

It would appear that there were then, as in this day, factional differences among the bodies of thought, where, unfortunately, prejudice was permitted to blind sober judgment, and personal animus to warp scientific conclusions.

*This commission, therefore, attributed the improvement in the afflicted peasantry, not to elimination of corn as a food, but more hygienic methods of living.

'Twas ever thus.

To give an idea of the amazing spread of pellagra during those years, it might be mentioned that, in the province of Vicenzo, the number of known pellagrins between 1853 and 1855 was 1380; in 1860, 2974; and 1879, 3400. These figures covered only one province.

In 1879 it was estimated that the number of peasants suffering with pellagra had reached the appalling number of 97,855, being distributed as follows: Lombardy, 40,838; Venetia, 29,386; Emilia, 18,728; Tuscany, 4382; Marches and Umbria, 2155; Piedmont, 1692; Liguria, 148; Rome, 76.

In Lombardy, where the disease always seemed to flourish most, the worst infected centers were Buscia, Pavia, Piacenza, and Ferrara. Next to Lombardy, it was most severe in Venetia and Emilia. In these three provinces the number of pellagrins in 1880 formed about 30 per 1000 of the whole agricultural population. This was also reflected in the military reports from those provinces, for from 18 to 20 per cent. of the conscripts were reported unfit for duty on account of illness of this character. Furthermore, in Italy, there were, in 1874, 945 pellagrous lunatics. In 1877 there were 1348.

The years 1871 to 1884 showed the "high-water mark" of this disease, 104,067 being officially reported. There was but little fluctuation in the figures until 1899, when there appeared a noticeable decline among the afflicted peasantry.

In a government report "Analli di Agricoltura, No. 18," which, to an extent, corresponds to the bulletins issued by our Public Health and Marine Hospital Service, is published the melancholy pellagra statistics for the St. Clement's Hospital of Venice for a period of six years

preceding, and it shows, with frightful distinctness, the extent of the "el delirio della miseria," as the Italians call it:

	Total number insane.	Pellagrous insane.
1874.....	558	178
1875.....	595	153
1876.....	666	175
1877.....	802	215
1878.....	859	294
1879.....	924	337
Total.....	4404	1352

In 1884 conservative estimates placed the number of pellagrins in Italian hospitals and insane asylums at 10,000, and the civic burden was so onerous that a bill, aimed at the prevention, was introduced in the Chamber of Deputies at Rome through the efforts of the Zannardelli cabinet in 1902.

In 1903 there were thought to be about 60,000 cases in Italy proper, though some of the statistics were unreliable. The last census of 1905 shows but 55,000 pellagrins in that country, and well-posted observers consider that this number has remained almost stationary up to the present date.

There are several reasons mentioned by Dr. L. W. Sambon which militate against correct reports; the patient does not always admit having pellagra; there is no compulsion requiring the authorities to be notified; and, not the least important, is the fact that local pride and a desire to show a decrease in a given locality cause the knowledge of some cases to be suppressed. Sambon, therefore, thinks that at present a fair estimate of pellagrins in Italy would be 100,000, though he admits that the mortality is not near so great as formerly. This briefly but fairly covers the situation in Italy.

In France, too, pellagra has wielded an important place in history. First reported in the vicinity of Arcachon in Gascony in 1818, it steadily spread along the coast of the Gironde and the Landes. Marchand, in 1826, called attention to its prevalence in the southern provinces of France. Dr. Petit, an observing French physician, of that locality, noted it about 1828, stating that it was more common in the Landes than in the Gironde district, and that at one time there were about 200 cases in a population of 6000.

According to Dr. C. H. Lavinder, it was first observed in France by the elder Hameau in the vicinity of Teste in 1818, whence came the French appellation "maladie de la Teste."

From these districts, the malady spread along the left bank of the river Garonne and toward the Pyrenees Mountains. Fortunately for the people in the vicinity of Dax, the disease never assumed serious proportions there.

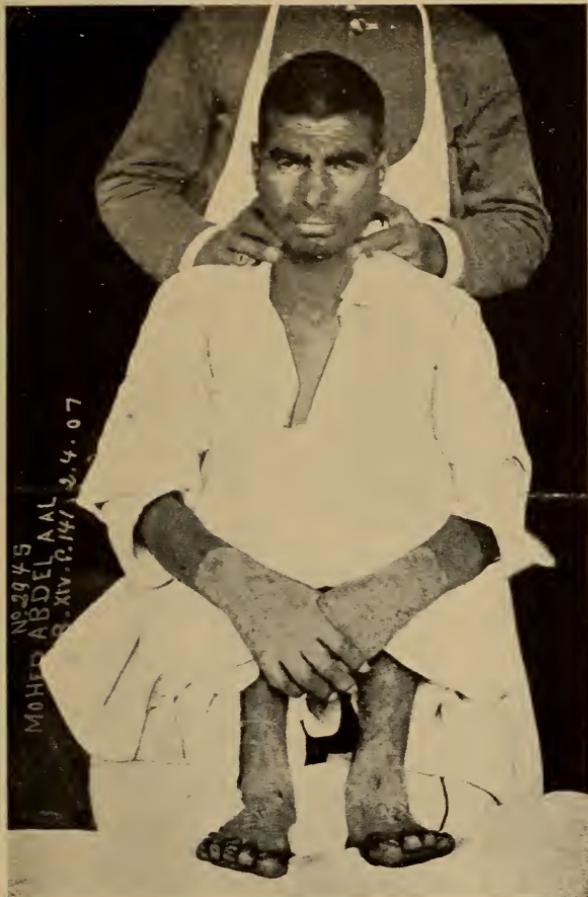
From 1829 to 1880, pellagra was one of the live subjects in the sociologic thought and literature of France. But, as remarked by Regis, there suddenly came a silence, and for the last thirty years but few cases have been reported. This sudden change is hard to explain. Some think that it has simply disappeared, "like the figment of a vision, leaving not a rack behind"; others think that there has been established a gradual immunity, or that the people have become so habituated to it that they have lost both interest and fear, viewing it with that fatalistic indifference of the Oriental.

At any rate, pellagra is no longer noticeable in France to any extent. Happy country!

In Spain, according to Triller, in spite of intelligent



Egyptian case of pellagra, taken after death. (Courtesy of Dr. F. N. Sandwith.)



Egyptian case of pellagra, showing symmetric "gauntlet" and "anklet"; also showing the pellagrous "breast-plate" observed in those whose breasts are habitually exposed to the sun. (Case of Dr. Sandwith.)

prophylaxis, this disease at present affects fully 20 per cent. of the inhabitants of certain provinces. It should not be forgotten that here, in the Asturias, pellagra was first described in 1735.

Casal spoke of the conditions there as follows: "Corn is the principal food of the laborer there; soups are made of it, to which they usually add milk; they likewise eat eggs, fish, and cheese; very rarely they buy fresh meat and occasionally salt meat."

"Here, as elsewhere, they begin by misconceiving the real origin of the affection," for different writers attempted to prove that it came from leprosy. Their hypotheses, of course, were not proved.

In Roumania the first recorded case was in 1810, and it seems comparatively easy to trace the progress of the disease along with the importation of wet and damaged corn by the inferior vessels of the coastwise trade.

From the period between 1833 to 1846 pellagra attracted much attention, and was called by the people "Buba Tranjilar."

Between 1854 and 1859 the government began to take notice, finding 4500 recognized cases in Moldavia and Wallachia. In 1885 this number had grown to 16,260, and in 1886 to 19,797.

In 1898 the peasant population of Roumania was estimated at 5,300,000, and the statistics pointed to 21,000 pellagrins among this number.

In 1906 Triller thought there were at least 30,000 there, and in 1907 other observers estimated the number at 40,000.

Corfu, one of the Ionian islands, famed in song and story, has also suffered the burden of this affliction. It

became epidemic there in 1856, and at this day exists in 30 out of the 117 communes. The percentage of pellagrins in the whole population is probably 3.2 per 1000 inhabitants. Typhaldos, of Corfu, has given the disease much study, and from him we have gotten some valuable information from many viewpoints.

Austria has not been exempt, for in the Tyrol, especially in Bukowina, having a population of 38,000, 2.9 per cent. are pellagrous. In this region of Austria there are seventeen institutions, where the peasantry can get proper food, and receive instructions as to cooking, hygiene, and other helpful knowledge.

This country has deeply considered the situation in its legislative assemblies, has enacted wise laws, restraining and educational, and seems to have the disease well in hand.

In Great Britain, only two cases were reported up to 1913, one by Drs. Brown and Carruthers, of Rock Ferry, and the other by Drs. R. Dods Brown and Cranston Low, assistant physicians in the Royal Edinburg Asylum. Since that date, however, Dr. Sampon has discovered many previously undiagnosed cases in England, 53 being observed in one hospital.

In Africa, as in other warm countries, this malady has gained a strong foothold. It was first recognized in 1847, by Pruner, who had observed it previously in Italy.

Pruner's statements did not meet with a favorable reception, for Hirsh and others "laughed him to scorn." Nothing further was said or done, until 1892, when, at a medical congress held at Cairo, Dr. F. N. Sandwith, senior physician and lecturer on medicine, Kasr-el-Ainy Hospital, Cairo, read a splendid paper on pellagra and its prevention.

He stated that, through the courtesy of Dr. J. Warnock, superintendent of the lunatic asylum of that region, he saw 40 or 50 pellagrous lunatics. Since 1893, Dr. Sandwith has seen more than 1100 cases, and asserts that it is quite prevalent in Lower Egypt, though not so much in Upper Egypt. He thinks that the proportion of those who lose their minds is not so large in Egypt as in Italy, though unable to explain why.

Dr. C. H. Lavinder, who has studied in Egypt also, rather differs from some of Dr. Sandwith's conclusions, mainly as to its slight prevalence in Upper Egypt.

Leaving for a time the consideration of this disease among the congested populations of the "Old World," we come nearer home, and still do we find the hideous face of this specter confronting us at every stage of our investigations. Suffice it to say, that hardly a country in Southern Europe has escaped, for Algeria, Tunis, Bulgaria, Servia, Portugal, Dalmatia, Croatia, Bosnia, Turkey, and even as far north as Poland, where freedom shrieked when Kosciusco fell, do we find it.

It will be most interesting to note the effect on the future prevalence of pellagra that may result from the European war now raging. These enlightening facts must, of necessity, be left to the historian of a later day.

In Jamaica, in 1888, Dr. Henry Strachan, senior medical officer, reported 510 cases of "malarial multiple neuritis," observed in the Kingston, Jamaica, Public Hospital, and on 121 of these patients full notes were taken.

"The patients complained of numbness and burning heat in the palms and soles, often accompanied by cramps, worse at night and in wet weather. Impaired vision and

hearing were noted, and a feeling of constriction around the lower part of the chest. An eczematous condition appeared on the tops of the eyelids, the angles of the mouth, and the mucocutaneous margins of the nostrils; the lips were usually red, and the palms hot to the touch and hyperemic. Later, motor pains of upper and lower extremities appeared. Pain was constant, especially of the feet. Emaciation developed with the progress of the disease. Pigmentation of the palms, lips, and soles was present; respiration was impaired, and death ensued from paralysis of the respiratory muscles. Death was rare, recovery being the rule.

"Soreness of the mucocutaneous borders, *i. e.*, eyelids, lips, urethra, anus, vulva, etc., was almost the first symptom. Wasting and contraction of the muscles was very marked in extreme cases, the 'claw hand' and foot being pronounced features. . . . In the last stage, when the patient is greatly wasted, there may be delusions with feeble attempts at violence. In this condition they may be committed to asylums.

"The eyelids are red and irritated; a slightly eczematous condition develops at the corners of the mouth and round the margin of the nostrils, with a fine branny desquamation. . . . The lips and buccal cavity are hyperemic, and there may be loss of surface epithelium on the tongue. Palms and soles are hypermic, due to dilated arterioles, and later they are deeply pigmented, the color varying from brown to intense black. The gait is typically ataxic. The disease attacks both sexes, youths and adults." (Marie.)

For quite a while this was called "Strachan's disease,"

but, in the light of present knowledge, we may safely class it pellagra.

Dr. Patrick Manson, in writing on "beriberi" (Tropical Diseases), takes issue, and in a foot-note writes as follows: "Dr. Strachnan has described a form of multiple neuritis which he calls malaria. The disease is endemic, and very common in Jamaica. It differs from beriberi, inasmuch as it is not attended with edema, is frequently attended with implication of the cranial nerves, and is rarely fatal. We have no account of any similar disease of other tropical countries. . . ."

Dr. G. L. Manning, the medical superintendent of the lunatic asylum at Barbadoes, has reported similar cases there, and thinks the trouble contagious, recommending the isolation of all patients.

Dr. D. J. Williams, of Kingston, Jamaica, writes, "The existence of pellagra was recognized here about twelve years ago, but as then it was unknown in the West Indies, and the correctness of the diagnosis was questioned, and the erythematous condition of the exposed limbs attributed to sunburn.

"Four or five years ago the disease was very prevalent. . . . With generous diet, rest in bed and tonics, the majority improved temporarily; others made no improvement, but suffered from chronic diarrhea, progressive weakness and emaciation, until death ended the scene."

. Mexico, Brazil, Uruguay, and the Argentine Republic have had their share of pellagra, though from some of these countries the reports are hazy and indefinite.

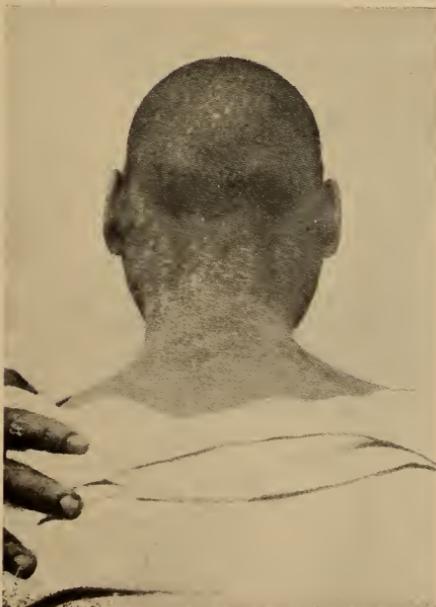
A graphic account concerning conditions dietetic and pellagrous in Yucatan, Mexico, has been furnished by Dr.

G. F. Gaumer of Izamal. He writes, "In 1882, in Yucatan, locusts destroyed vegetation, especially Indian corn. Corn being the only cereal used in Yucatan for bread, famine seemed inevitable, until the merchants began to import it from New York. This importation continued till 1891, when the country had recovered from the devastation of the locusts. The imported corn was brought in the holds of vessels as ballast. By reason of exposure to heat and humidity on the voyage, the corn underwent fermentation and became unfit for food. The constant eating of this spoiled corn led to the slow development of pellagra.

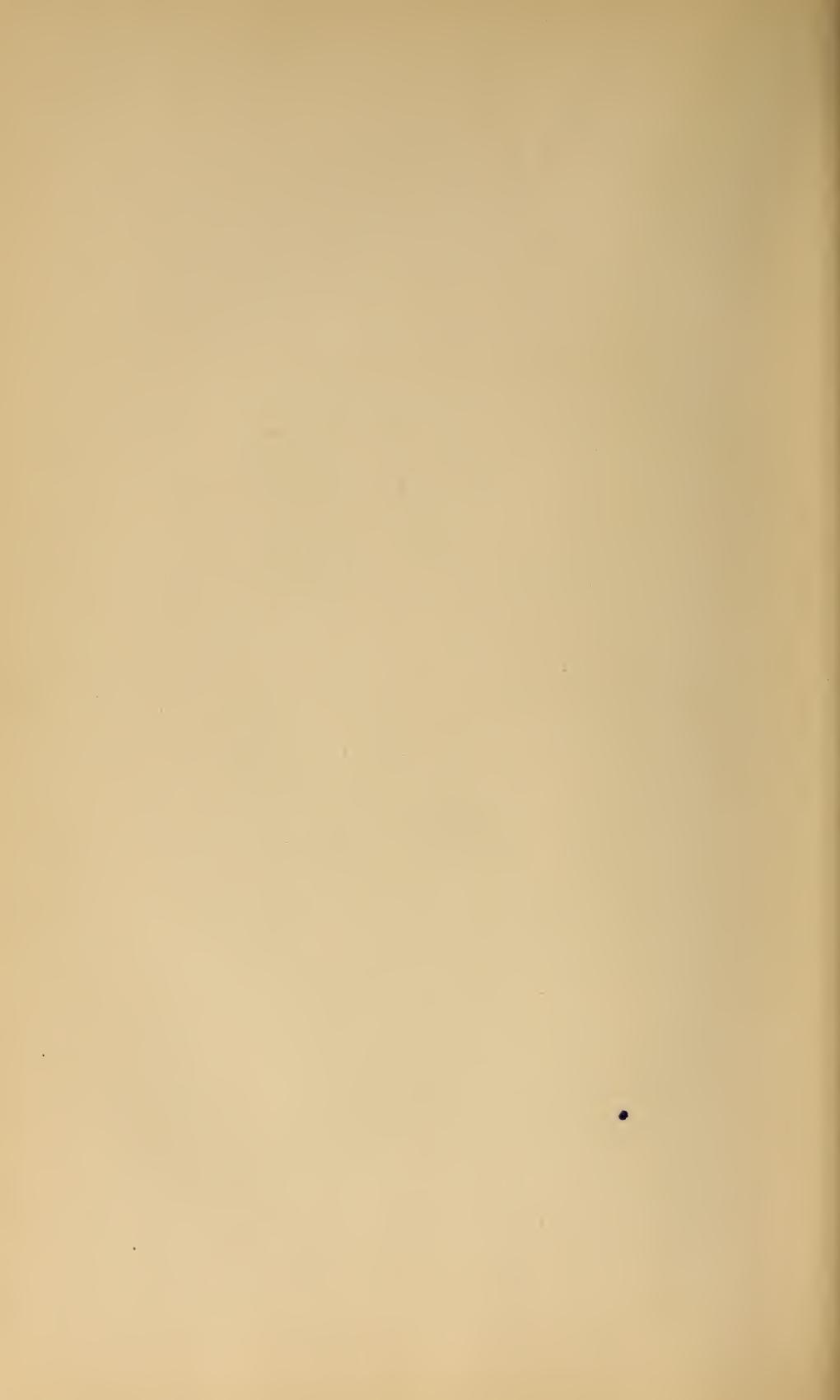
"The disease was confined to the lower and middle classes, who were obliged to purchase the cheapest corn in the market. The wealthy classes escaped, as they did not eat the imported corn. For the next ten years, 1891 to 1901, Yucatan produced enough corn for home consumption, and cases of pellagra no longer developed. The old cases ran their course fatally. From 1901 to 1907 the corn crops were almost total failures, and corn was again imported in larger amounts than ever before. Mobile and New Orleans were the chief sources of supply, but some came from Vera Cruz—all by water. Again pellagra became epidemic, but was not confined to the middle and lower classes as before. It had been found more profitable to raise hemp than corn, so all classes used the imported cereal. Consequently, pellagra spread alike among the rich and poor. At the close of 1907, 10 per cent. of the inhabitants were the victims of pellagra, and in August, 1909, not less than 8 per cent. of the population had the disease."



Egyptian case of pellagra. Note the "breast-plate" on exposed surface of breast.



African case of pellagra, showing erythema on back of neck and shoulders.



CHAPTER II

PELLAGRA IN THE UNITED STATES

As early as 1863 two cases were recognized in New York and Massachusetts—one by Dr. John P. Gray, of Utica, New York, and one by Dr. Tyler, of Somerville, Mass. It might not be amiss to mention that, at this time, there were reports of a supposed epidemic of pellagra near Halifax, Nova Scotia, though details were lacking and the diagnosis was only inferential.

We now come to the discussion of certain conditions in some of the large detention camps or prisons during the late Civil War. More particularly, may we revert to Libby Prison, at Richmond, Va., and the Andersonville prison, both used for Federal prisoners, though the former was mainly for officers, and the latter for private soldiers.

The war was dragging its weary length, both sides were embittered by the internecine strife, and both had severely taxed their resources to carry on the conflict.

Far be it from the writer to enter into any discussion of any issues involved, or the wisdom or unwisdom of measures employed in the management of these prisons.

It is well known that the mortality was frightful.

Right at that time the South was staggering in the struggle for governmental existence; all sustaining indus-

tries were paralyzed, and it was a problem to find sufficient sustenance for her own soldiery and people, with the added burden of providing for all these prisoners. Corn was the principal, sometimes the only available, food to be had, and the facilities for transporting and preserving it were far from ideal.

The writer has been able to interview several veterans of intelligence, who were at Andersonville during that dreadful period—two who were guards and one who was a prisoner—and the details, even softened by all the years of healing time, were harrowing in the extreme.

The hygienic facilities were primitive, nor was much effort made to enforce those supposed to be in vogue. A major part of the diet was of corn products, some of which had been through more than one wetting and drying, and which were mouldy or wormy. The water was bad, the surroundings were depressing, and these poor men suffered the pangs of illness, to which were added the sorrows of nostalgia—that dread of wanderers far from home.

Little wonder it was that they sickened and died, and fortunate the few who, "by reason of strength," were able to withstand the noisome odors, the scanty and unwholesome food, and the depressing influences on every side.

Dr. J. W. Kerr, of Corsicana, Texas, has written a report of some of the conditions, and, in the light of a clearer retrospective vision, he believes that pellagra was the evil agent responsible for many deaths.

The veterans mentioned above have told the writer how the men had a supposed eczema; how they loathed their food, and how it served them after it was eaten; how

their skins were rough and hard, and how their hands were sore and cracked; how their bowels were chronically loose —so much that there was a pathetic joke that a prize would be given any prisoner having a solid fecal movement. Upon this weight was superimposed the melancholy deepening into the different forms of dementia, where indifference to fate brought about increased carelessness as to common rights in their adversity, or hygienic precautions that would have ameliorated the common lot.

Whether or not this was really pellagra will probably not be positively known, but there is a widespread belief among students of history that such was the disease which brought to an untimely end many of the flower of the Federal army.

From 1864 up to 1883 we hear nothing more of this disease, when one case was reported by Dr. S. Sherwell, of Brooklyn, New York, in a Genoese sailor.

Dr. H. N. Sloan asserts that pellagra was diagnosed in the South Carolina Asylum at Columbia in the early '70s, but no written nor printed record has been found. Dr. D. S. Pope, of Columbia, as quoted by Dr. Babcock, is satisfied that at least two cases occurred in the South Carolina penitentiary in the middle '80s.

In 1889, Dr. Bemis, of New Orleans, left a written diagnosis of a case in a white woman at the Charity Hospital in that city.

During all these years it is practically certain that pellagra existed plentifully in the Southern States under various diagnoses. Such puzzling cases were diagnosed as unusual manifestations of tuberculosis, syphilis, malaria, acute delirium, dementia, melancholia, hook-worm, ec-

zema, dermatitis exfoliativa, and others. In some quarters, somewhat removed from the medical centers, where the niceties of diagnosis were hardly appreciated, some of the appellations applied to undoubted cases of pellagra would have been humorous, had they not been fraught with dangerous consequences for the sufferers. "Elephant itch," "seven-years itch," "country scurvy," "poison oak or ivy," but, most of all, *eczema*, that medical mantle that covers so many slipshod diagnoses.

The writer well remembers a case occurring in a mulatto girl twenty-two years ago, the manifestations of which he was unable to understand at the time, but which seem plain in the light of present knowledge.

This girl, an intelligent school teacher, twenty years of age, was treated for diarrhea, indigestion, and nervousness during the months of March, April, and May. Her diarrhea and indigestion improved, but she remained nervous and averse to work all the summer. That fall and winter she seemed well, but in the following March her diarrhea returned worse than before, with the other attendant symptoms magnified. She also had an "eczematous" eruption on her hands and feet, symmetric and sunburned in appearance. She was much depressed mentally, so that she gave up her school, and changed her home, with the hope that new environments would help both her digestion and mental condition. She seemed to improve, and, by November, she returned, apparently well, though reduced in weight.

The following March showed a renewal of every symptom in aggravated form, with rapid emaciation, frequent involuntary stools, hands and feet first erythematous, then

raw and weeping, a settled melancholy, and death in the early part of May.

This patient was seen by some well-posted physicians, but none of them were able to make a diagnosis.

In 1900, the writer saw two fatal cases of this sort—one in his own practice and the other with a confrère—both of whom gave a history of recrudescences and exacerbations through several preceding years.

All of these patients were in agricultural districts, were in limited circumstances, and had always eaten corn-meal.

With the slight exceptions mentioned, the pellagra situation remained in *statu quo* until 1902, when Dr. H. F. Harris, of Georgia, reported a case.

As has so frequently happened to the prophecy of a prophet in his own country, the report of Dr. Harris excited but little comment, and practically nothing more was heard of pellagra until about 1907, when independent reports from various sections of the South began to come in. Medical officers of asylums in South Carolina and Alabama reported such cases with scientific exactness, and in the summer of 1908 Drs. Babcock and Watson, of Columbia, S. C., went to Italy to study the disease.

On their return, they were able to positively identify it, and, as they wrote of it, others began to remember cases in practice of past years; cases not diagnosed; cases whose deaths were hard to explain.

In rapid succession, pellagra was then reported from Wilmington, Morganton, and Charlotte, N. C.; Augusta, Milledgeville, and Atlanta, Ga.; Tuscaloosa and Montgomery, Ala.; Columbia and Charleston, S. C.; and many other places in a number of states.

In 1909, the people of the South, as well as the officials of the Public Health and Marine Hospital Service, who had already made valuable investigations, began to wake up to the gravity of the situation, and in November, 1909, a Conference on Pellagra was held under the auspices of the South Carolina State Board of Health at the State Hospital for the Insane, Columbia, S. C. Another Conference on Pellagra was held at the same place in October, 1912, which assumed a national importance.

At these conferences representative men, physicians, publicists, students of sociologic problems, and citizens of every walk of life attested their interest by their presence.

The discussions and deliberations as to the etiology, pathology, and clinical aspects of this disease will receive attention; suffice it to say, that the ear of the American people was reached, and pellagra, as an American problem, was driven home to the most skeptical.

Since that time, up to the present writing, the question has been not one of fact, but of degree. At that time about 1000 cases had been reported from thirteen states, but, as the returns have come in, practically every state in the Union reports within its borders either positive or suspected cases.

In some of the states the existence of pellagra has received much more than passing notice, as attested by many and valuable contributions as to its features as it has appeared in different localities.

Dr. J. N. Hewett, of Lynnhaven, Va., and Dr. Beverly Tucker, of Richmond, have studied many non-institutional cases in their and adjoining states, being convinced that it exists to a far greater extent than is commonly realized.

In only a very few states is the occurrence of the disease required to be reported, and in the absence of records of cases it is quite impossible to know how much of the malady exists; and that of the states in which the disease is notifiable the only one which is really getting reports is the state of Mississippi, where the number of cases reported during the last three months of 1914 were as follows:

October, 1914	824 cases.
November, 1914.....	603 cases.
December, 1914.....	418 cases.

Among the states where pellagra has assumed formidable proportions are Virginia, North and South Carolina, Georgia, Florida, Alabama, Mississippi, Louisiana, Texas, Tennessee, Illinois, Missouri, Kentucky, and Arkansas. In others, the health officers are on the watch for sporadic cases, but do not seem to locate very many.

That some of these returns are incomplete is in many instances shown on their faces. For instance, Florida reported only 50 cases up to 1911 in the whole state. The writer alone had, in that year, seen 18 cases from that state that came to this city from Florida for treatment. If that many came to one city for treatment, the inference is plain that there must have been many more than 32 who remained at home.

Again, there is a sentiment springing up in some quarters that pellagra is a "loathsome disease," and one in which the afflicted pellagrin does not wish the public to know its presence.

A short time ago the writer treated a widow lady, who, when she was informed that her trouble was pellagrous,

earnestly requested that her son be not informed what was the matter. She seemed to feel ashamed of her ailment, nor could she be reassured by any persuasive arts of her medical attendant.

A lady from Florida recently was in Atlanta for treatment, and, upon the rumor that she had pellagra becoming rife in the family hotel where she boarded, some of the boarders rose in arms, insisting that if the proprietress did not ask her to leave, they would seek other homes. She was asked to leave, and did so.

Many of the public hospitals and sanatoria have passed rules excluding pellagrins, and can it be wondered that these unfortunate invalids use every effort to keep from general knowledge the real nature of their malady?

In more than a few instances the statement to an inquiring patient that pellagra was the diagnosis has brought forth expressions of either incredulity or indignation, followed by impassioned appeals that no one be informed of the nature of the illness.

Many times the patient, with an assumed skepticism, goes to the family physician, carrying the plainly-implied desire that the diagnosis be not verified. The physician, being anxious to give his troubled questioner the benefit of every doubt, admits that perhaps there is a mistake, and, upon this figment of uncertainty, the patient boldly asserts that a mistake has been made, that only an "eczema" causes the eruption, that some dietetic errors are responsible for the gastro-intestinal manifestations, and that something else is behind the nervousness.

To place this patient in the pellagra column would, if known, excite a stormy protest.

This picture will bring to many readers the memory of just such a state of affairs, and can we wonder that reliable statistics are hard to obtain?

The writer, from exhaustive inquiry among health officers, asylum superintendents, and other interested observers, believes that a present estimate of forty thousand pellagrins in the United States is not far from correct.

"Like appendicitis, the disease is now better diagnosed—hence the seeming rapid increase; although, for some unknown reason, there is probably a real increase, but not so great as it appears." (Babcock.)

It would be puerile for any of our states, no matter how far north, with a "holier than thou" attitude, to disclaim its presence, or to minimize the reality of the problem now at our doors.

Not so many years ago the late Grover Cleveland uttered that epigram, "A condition and not a theory confronts us," and well may we apply those words to the visitation of this malady that, unless checked, will bring sorrow to many hearthstones and disquietude to many municipalities and states.

CHAPTER III

A DISCUSSION OF THE ETIOLOGY OF PELLAGRA

It is with a sense of trepidation that the writer enters into the discussion of the etiology of this disease. That spoiled maize was an etiologic factor was suspected by Casal, who, in 1762, attempted to elucidate the causal relationship between the corn and the "mal de rosa," as he dubbed it.

This suspicion remained somewhat quiescent, though not entirely absent, until Mazari formulated a theory that the disease was brought about by the lack of certain nutritive qualities in corn.

About this time, two schools of thought arose, the one espousing the "Zeist" theory (from *Triticum spelta*, or *Zea Mays*), the other opposing it.

For many years a spirited, sometimes acrimonious, battle raged between these two schools, the echoes rising and falling like the swell of an ocean, as greater or lesser minds engaged in the wordy conflict.

Had this chapter been written in 1912 or 1913 the writer would have hesitated in devoting much space to the "Zeist" theory. At present, however, the trend of opinion is departing from the belief that pellagra is transmitted by a winged, blood-sucking insect, and is leaning more toward the idea of its etiology lying in an unbalanced diet con-

taining an excessive proportion of corn or corn products, with other cereals and vegetables.

For this reason it is still of interest to study the early history of maize, its distribution, and food consumption. The chemistry of spoiled and sound corn also will be considered.

Maize is a plant of the tribe Maydeæ, of the order Gramineæ or grasses. It is unknown in the native state, but is probably indigenous to tropical America. Small grains of an unknown variety have been found in the ancient tombs of Peru, and Darwin found heads of maize embedded on the shore of Peru at 85 feet above the present sea level.

Bonafous, however (*Histoire naturelle du maïs*), quotes authorities as believing that it originally came from Asia, and maize was said by Santa Rosa de Viterbo to have been brought by the Arabs into Spain in the thirteenth century. A drawing of maize is also given by Bonafous, from a Chinese work on natural history, dated 1562, a little over sixty years after the discovery of the New World. It is not figured on Egyptian monuments, nor was any mention made of it by Eastern travelers in Africa or Asia prior to the sixteenth century.

Humboldt, Alphonse de Candolle, and others, however, do not hesitate to assert that it originated solely in America, where it had been long and extensively cultivated at the period of the discovery of the New World, and that is the generally accepted modern view.

Passing the purely botanical aspect of the stalk and outer covering of the grain, or husk, which does not concern us here, we find that Indian corn is a very nutritious

article of food, being richer in albuminoids than any other cereals when ripe (calculated in the dry weight). It can be grown in the tropics, from the level of the sea to a height equal to that of the Pyrenees, and in the south and middle of Europe, but cannot be grown profitably in England. It is extensively grown throughout India, and is the most common crop throughout South Africa, where it is known as *mealies*, being the staple food of the natives.

As an article of food, maize is one of the most extensively-used grains in the world. It contains more oil, too, than any other cereal, ranging from 3.5 to 9.5 per cent. in the dried commercial grain.

Sound, matured, and well-dried corn is one of the most available, as well as most nutritious, of the foods offered the human race. Under proper methods of transportation it can be hauled an indefinite distance without deterioration; and, when properly gathered and marketed, it will remain sound and wholesome for years.

On the other hand, no grain is more susceptible to unsanitary influences or careless handling.

That the eating of spoiled corn has made a decided impress on the language of the Italians may be judged by the names given in different dialects to express its odor—*scagni*, *muffito*, *patti*, *sobbolli*, *verdet*, *butta*, *arbolli*, *smaserido*, *romatico*, *mofflet*, etc.

On gross examination by the ordinary observer, spoiled corn may be distinguished by its cracked or wrinkled hull, its color of old gold, its lack-luster appearance with embryo enlarged, blackish, and showing through the surface like a ship in a fog. It nearly always shows external spots of a brownish or greenish color like verdigris.

If the grain is cut in half and examined, the perisperm shows brownish, and the embryo a dingy black, instead of the white of good grain. The mass of the perisperm is often eaten away, leaving a little cavity in which is found the coleoptera nesting there, and a fine dust can be shaken out of the grain. These coleoptera are called "corn weevils" by the laity, and corn so affected is considered unfit for human food.

The embryo is nearly always atrophied, so that it does not fill out its normal place between the perisperm and the hull of the caryopsis. Sometimes the outward appearance of the grains seems normal, but there can be noticed, on close inspection, little eroded points scattered over the surface, favoring the development of some of the moulds. From this also comes a greenish dust, which seems to penetrate the interior of the grain. In many grains the appearance of the moulds and the *acarus farinae* coincide.

The meal made from spoiled corn is not always easy to detect, unless it is decidedly bad. When much damaged, it gives off a "musty odor," sometimes slightly aromatic, and has a bitter taste.

Several tests for spoiled corn are mentioned by Marie, which are said to be fairly conclusive. He says, if some grains of spoiled corn are digested in 90 per cent. alcohol, their grayish-yellow color changes to an intense red, the alcohol becomes red, and the color deepens with time. On the contrary, if the grain is sound, it does not change color, even if it remains in the alcohol for two months, though the alcohol becomes yellow.

Again, if in a dilute solution of caustic potash the hull of the grain of spoiled corn becomes first reddish brown,

later all the solution becomes brown, and gives off a penetrating odor of spoiled corn. The more the decomposition of the corn has advanced, the more decided is the reaction. If this alkaline fluid is neutralized by tartaric acid, flakes of a coffee color are precipitated which have the odor of spoiled corn; these flakes are insoluble in water or ether, but soluble in alcohol. This reaction, according to Marie, can be obtained with both meal and bread made of spoiled corn, the reaction showing a lemon-yellow color.

Following the experiments of this investigator, we find that the tincture of spoiled corn yields three substances. The first is, at ordinary temperature, a liquid of ruby red color, with a bitter taste, and an odor of decayed corn. It is soluble in alcohol and ether, but insoluble in water, in which it floats; it becomes resinous when exposed to air, and does not yield a precipitate with the iodid of potash, nor with other metallic salts. With caustic potash and benzin it yields a bright yellow precipitate, and a drop of it on paper makes a greasy spot. This tincture contains the oily substance of corn, and may be called the *red oil* of spoiled corn.

The second substance is a reddish brown, styptic and bitter, is soluble in ordinary alcohol, but in absolute alcohol it precipitates yellowish flakes, which dissolve quickly if a little distilled water is added. It is also insoluble in ether, and yields, when treated with iodid of potassium, a flaky precipitate; with sulphate of copper it becomes green; if treated with much water, it separates into two parts, one of which, insoluble, is precipitated in the form of a brown amorphous powder; the other makes a bright yellow

solution. This interesting product is called *pellagrocein*, or the *toxic substance* of spoiled corn, and its toxic properties are very marked.

The third substance, when heated with ether, solidifies into a mass, which becomes hard on exposure to the air. It is soluble in diluted alcohol and in a solution of caustic potash, but in water, benzin, or absolute alcohol it is insoluble. When heated it becomes soft, and can be drawn out like wax. This is the *resinous substance* of spoiled corn.

It may be interesting to note that the substances obtained from spoiled corn are analogous to those obtained from spurred rye, possessing the same oxytocic properties.

A great number of micro-organisms have been found in spoiled corn by investigators on "both sides of the water," and it would not be profitable to enter into a description of them all, but the more important will be considered.

Sporisorium Maidis.—This is the best-known parasite of spoiled corn. Its isolation and description inaugurated a new era in the study of pellagra in Italy. Seen under the microscope, it is of a greenish color, resembling little globules, but not coherent.

Balardini, who first isolated and experimented with this micro-organism, found that when eaten for a while by man, it would produce gastritis and diarrhea.

It has been common knowledge among the laity for many years that "musty meal," or spoiled corn, would cause illness in man or beast; and the writer remembers how, when a lad, his mother lost many fine chickens from a mysterious malady, which was solved when the cook

was discovered to have been feeding the fowls on dough made from spoiled meal.

Lombroso did not think this organism responsible for pellagra, however, because he could not find it often in Lombardy, but others have thought differently.

Probably the most important fungus is the *penicillium glaucum*, which, while it forms on other grains besides corn, does not in them seem to produce the pellagra poison, and is not of itself toxic to the human system.

It is observed in pendicular filaments, from which are developed many flaky conidia. These filaments compose the greenish-blue dust, which is often noticed on the grains of spoiled corn. It does not long remain on the surface, but, when the corn is not housed in dry quarters, seems to penetrate into it.

Says Lombroso, "Pellagra does not come directly from the *penicillium*, but from the *pellagrozeina* (identical with strychnin), formed in the corn as a result of the action of the *penicillium*.

Other micro-organisms of probably less importance are the *oïdium lactis maidis*, *eurotium herbariorum*, *sporothrichum maidis*, *bacterium maidis*, and the *aspergillus glaucus*, the last of which is found in the same conditions as the *penicillium*, but more rarely.

The *bacterium maidis* has not been found alone in faulty meal, but has also been found in sound, and in the bread made from such meal.

"In 1881 Majocchi found a very motile bacterium in both sound and spoiled corn, but always in greater number on spoiled corn—this micro-organism he called *bacterium maidis*, and he thought he found it in the blood



"A Lombroso chicken." This fowl was fed for four weeks on spoiled meal. (Courtesy of Dr. H. P. Cole, Mobile, Ala.)

of seven pellagrins in the first stage of the disease. Cuboni, working with this micro-organism, found it constantly and abundantly on spoiled corn. He also called it *bacterium maidis*, and recognized its similarity to the *bacterium termo*, though it resisted a higher temperature." (Marie.)

According to most observers, this bacterium occurs more readily in damp or immature corn, its development being arrested by drying, though on each fresh wetting of the grain it can renew its development. This explains why corn can be partly "sweetened," and then, on exposure to dampness or other unfavorable circumstances, can again become unfit for food.

Cuboni thought that the intestines of pellagrins offered an exceptionally favorable soil for the propagation of these bacteria, while they did not thrive so well in the intestines of healthy individuals.

Paltauf and Heider have concluded from their studies that the *bacterium maidis* is the original potato bacillus, transplanted to a new soil and christened with a new name. They are not alone in this view.

As in other grains where there is a large percentage of starch, the saccharomycetes are numerous in spoiled corn, but fermentative processes are necessarily due to other causes, and may, to an extent, be ascribed to the *bacterium termo*.

Much study has been given to the different moulds on spoiled corn, but not many observers in America have followed it up. To our painstaking friends, the Italians, we owe most of our information on this subject, though the French have not lagged far behind.

Monti and Tirelli, using the methods of Koch, have made some very interesting studies of this subject. They found fourteen different organisms, some of which have already been specified (one of them the potato bacillus under its own name), and they opine that none of these are capable of directly injuring the human organism, but all are capable of inaugurating decomposition in different cereals. None of these organisms flourish when the grain is kept dry, but require a certain amount of moisture, and, in some instances, a variable degree of heat, in order that they may develop.

The *penicillium glaucum* will flourish at a lower temperature than most of the others, and consequently it is more often present. For this reason it has possibly received undue importance.

Many experiments have been made with the bacterium *maidis* by Lombroso and others. Into white mice the alcoholic extract of corn-meal, infected with the bacillus, was injected. Doses of 0.5 c.c. were injected, producing coma, paralysis, and death at the end of about two hours.

Here are some other experiments made by Lombroso and his contemporaries, as narrated by Marie:

If cultures on polenta of one, two, six, and up to seven, days old are given to animals they become accustomed to it slowly; the initial diarrhea, which is the only symptom, may even cease; but cultures over four to five days old are refused, perhaps because of their bad and very pronounced taste. As a consequence of this nourishment, digestive troubles are produced, sometimes vomiting, almost always diarrhea, but never derangement of the sensibilities or of the motor system. At the end of some days the

weight begins to diminish, but then maintains itself within normal limits. The temperature is usually maintained at normal; in the first days only two cases showed a slight evening rise.

The attempt to cultivate this bacillus on wheat bread met with little success; two pigs, fed for fourteen days with this bread, showed no change.

An experiment was then made with the alcoholic extract obtained from a culture on polenta twenty-five days old. The extract, prepared by Prof. Fileti, was injected into three dogs, under the skin of the back, in doses of 5 per cent., 10 per cent., and 25 per cent. of the weight of the animal. The two dogs which had received the largest doses died two days later, after presenting the following symptoms:

Paresis of the hind legs, almost continual tremor, general depression, which was rapid and progressive, gradual loss of voluntary motion, complete paralysis of the hind legs, mydriasis, slight increase of temperature, acceleration of respiration and pulse, insensibility, bloody diarrhea, and death with prolonged agonistic state. At the autopsy edema of a hemorrhagic nature in the hypogastric region and the extravasations in the spleen.

The dog inoculated in the proportion of 5 per cent. of its weight exhibited at the beginning the same symptoms, but, at the end of the second day, his condition improved; however, the hind legs remained paralyzed, and the diarrhea continued for several weeks with a remarkable diminution of weight.

In the case of two other dogs, intravenous injections, in

a proportion of 5 per cent. of body weight, caused death after the development of the above-mentioned symptoms.

Injections into ten frogs, with corresponding doses, brought on death in three hours with paralysis, diffuse ecchymoses on the interior of the thighs and into the hypogastric region. Intravenous injections of the extract of sound polenta up to 10 per cent. had no evil consequences; the same may be said of the subcutaneous injections made in double doses.

After this somewhat lengthy discussion concerning corn, spoiled and otherwise, it will more interest the reader to plunge "*in medias res,*" and give in more intelligible terms the theoretic, if not real, connection between maize and pellagra.

Lombroso has been the high priest of the zeists, his arguments have been weighty and voluminous, and it has required a stout heart and a nimble wit to cope with him. Even since his death the material he left behind has proved the bulwark of the adherents of the maize theory as to the causation of this disease, and all that has been written or said has necessarily partaken of his arguments.

Dr. C. H. Lavinder, in a logical and fair discussion contributed to the New York Medical Record, traces from an early period the doctrine adduced by Balardini as to "verderame" up to the present, and the writer makes acknowledgments for the use of these statements.

The early views have been sufficiently covered, so the status of to-day may be given as follows:

"I. It is declared that history and observation show clearly that the first appearance of pellagra, and its later dissemination followed, more or less closely, the introduction

of maize culture into Spain and its gradual spread to France, Italy, and other countries of southern Europe.

"II. It is declared that pellagra is found as an endemic disease only in those countries where maize is grown, and extensively used as an article of diet by the poorer rural classes. It is of importance to note, on the other hand, that the area in which pellagra is found endemic is but as a spot upon the extensive area over which the maize is found under cultivation. There are vast tracts where maize is, and has been, grown as food for many years, and yet no pellagra has appeared. This is a matter of much import with regard to the etiologic rôle which spoiled maize is supposed to play.

"III. It is declared that countries in which maize is not grown or used as food, or only exceptionally so used, even though contiguous to pellagrous sections, or actually surrounded by them, are free of pellagra."

[Lombroso, Babes and Sion, and others have reported just such peculiar instances.]

"IV. It is declared that a change of food, either among individuals, or groups of individuals, brings constantly a diminution or disappearance of pellagra, or vice versa. There are also many reported instances of this kind. Most writers allege that recovery may take place, or amelioration occur in the condition of pellagrins, by removing from their diet all maize and maize products. The case of Corfu, in this connection, is regarded as such a notable instance that it will bear quoting. Typhaldos (whose study and contributions to the literature of pellagra have been previously mentioned) states, that pellagra was unknown in this island previous to 1857, and that up to

that time the inhabitants grew their own maize, which was of a fine quality, but, for economic reasons, the culture of grapes became almost universal, and they began to subsist on the imported maize of very poor quality—that is, spoiled maize. Pellagra followed and became endemic, and he found, in 1866, 81 cases there."

Lavinder next groups the various modifications of the maize theory in the following lucid manner:

"I. The idea that maize, as a food stuff, is wanting in proper nutritive value. This conception is in reality no longer held, having been rather effectually discredited by many careful analyses of maize, which show that this cereal possesses high nutritive value, is rich in fats and nitrogenous substances, and is easily assimilable."

The chemical analysis and statement of the dietetic value of corn in the beginning of this chapter show that the argument concerning the deficiency in its nutritive value is entirely fallacious. The writer, in some dietetic observations conducted several years ago, found that laboring men, on a diet of corn-bread alone, could for as much as a week keep squarely up to their standard of efficiency. He was unable, however, to keep them on this diet over a week, not that they were suffering from any physical infirmity, but simply because they desired to return to their regular "bill of fare," and the persuasion of the writer was not effective enough to control them.

In food value it compares very favorably with rice, for example, which constitutes a staple article of diet among the numerous classes of people who do not suffer from pellagra. Pellagra is, moreover, not infrequently found among well-nourished individuals, and its symptomatology is not that of inanition.

"II. The idea that good, sound maize contains certain toxic substances which cause pellagra. This is another view which has been largely discredited by the absence of pellagra in so many places where maize is, and has been, for long periods, extensively used as food.

"It is also worth while to note that the gross distinction between sound and spoiled maize, in the opinion of many able observers is not always easily determined. Maize, by reason of its high fat and nitrogen contents, seems quite subject to change under the influence of bacterial growth, and grain which to all appearance may seem perfectly sound can nevertheless be shown to be spoiled or damaged to a greater or less extent."

The writer well remembers how, when a lad, he used to observe the care with which corn was prepared when it was "milling day," how all nubbins or defective ears were rejected, and how the small ends of the ears were broken off, so that none but sound, well-matured corn was sent to be ground into meal. This custom obtained among all the farmers, for in those days the South raised its own food crops to a major extent, nor had the immense and fertile expanses of the "Golden West" assumed their position as "granary" for these states. The well-trained noses of farmers or housewives could detect the slightest foreign odor, and luckless was the miller who sent back musty meal in exchange for sound and wholesome corn.

Under this old régime there was no pellagra in the South, nor did it ever appear until, under changed conditions, brought about by economic reasons, as happened in the island of Corfu, other crops took the place of corn—other crops that brought more ready money, and the West was called on, as was Egypt in the days of Pharaoh.

In the Western and Middle States, as corn became a staple article, the problem was not alone to transport and sell it, but to house it in the immense quantities in which it was produced. The consequence was, that in many sections the corn was not permitted to mature in the fields, and await there until thoroughly dried before it was put in barns, but it was cut, and the corn on the stalks was "shocked" in the fields until it was convenient to market it. In this semi-exposed condition, subjected to all the varying changes of the weather, the corn waited sometimes for weeks, and then, perhaps, just after a season of rain, or when the atmosphere was humid in the extreme, it was put in close cars, and its journey began.

If, by good fortune, it reached its place of final marketing in wholesome condition, it had to run the gauntlet of different wholesale storage depots, of warehouses for the mills, where often dampness abounded, and micro-organisms found congenial environment for bountiful multiplication.

Thus, the corn, that was originally one of Nature's best food-stuffs, under the blighting treatment forced by commercial necessity and economic exploitation, became an object of suspicion in many quarters, and in others practically under the ban of conviction.

This, in brief, is the present status of corn—the commercial article whose safety as food is now on trial.

"III. The toxicocochemical idea, to continue with Dr. Lavinder, that under the influence of parasitic growths (bacteria or moulds) maize may undergo certain changes with the formation of one or more toxic substances of a chemical nature (exogenous poisons). This idea has a

host of adherents. It was established through the admirable labors of Lombroso, who, as said, has been its great advocate and exponent, and it is perhaps to-day the most popular of all the various phases of the maize theory. It is not without critics and antagonists, however, and Lombroso's experimental work and conclusions have been seriously called in question by many able students of the disease.

"For instance, if we use the bacterium *maidis* as an example, we may put it that it is inoffensive *per se*, but releases from the corn, after the peculiar toxicоchemical action, a ptomain that works the harm.

"The whole gist of Lombroso's argument may be expressed by the theory that in pellagra we are not dealing with a primary poison, but with an intoxication produced by poisons developed in spoiled corn through the action of certain micro-organisms in themselves harmless to man.

"Now, while Lombroso experimentally produced several poisonous oils and tinctures from spoiled corn, as described previously, unfortunately he could not incriminate any particular micro-organism. Many other adherents have followed up these investigations, producing in animals and fowls symptoms analogous to pellagra; but similar symptoms have also been produced by poisonous substances obtained in the same way from other cereals.

"Voluminous reports of such experimental work have been adduced by Erba, Hausemann, Pellogio, Gosio, Ferrati, Mariani, Belmondo, Pelizzi, Tirelli, and others with practically the same findings.

"It is of much interest in this connection to know that Babes and Manicatide succeeded in neutralizing the

toxicity of spoiled maize extract with the serum of cured pellagrins; and, from a series of carefully conducted experiments, concluded that the blood of pellagrins contains a substance which possesses the property of counteracting the toxic action of the extracts of spoiled maize."

The theory built up on this hypothesis has been extensively tried out, and at present has but few adherents.

"IV. The toxic infective idea, that from spoiled maize there are formed within the body certain toxic substances (endogenous).

"Neusser advocated the view that under some circumstances there is formed in maize, largely under the influence of the *bacterium maidis*, a certain 'receptive mother substance' which later, in the body, underwent a further change. Under other circumstances, however, he viewed the disease as a direct intoxication.

"De Gaxa attributed great importance to the action of the colon bacillus on ingested maize. His idea seems to have been that the vegetating properties of this bacillus may become greatly modified on a culture medium of maize, and he alleges that he has shown the production, by the colon bacillus on maize media, of specific toxic substances."

The tendency to charge the colon bacillus with various "high crimes and misdemeanors" has not been confined to Italy or France, for one eminent American gastro-enterologist has recently proved to his satisfaction that the colon bacillus alone is the microscopic malefactor in the production of pellagra.

Passing for the time from the discussion of spoiled corn and corn products as an etiologic factor in pellagra, we desire in fairness to present the other side.

In opposition to the "zeistic" doctrine there arose a school, especially in France, and a group of investigators, led by Landouzy, began to report cases of pellagra where it was claimed no corn had ever been ingested.

This brought to the fore Roussel, that deep thinker and trenchant writer, who questioned their observations, discredited their diagnoses, and introduced the new term "pseudpellagra," which he claimed fitted their cases.

The term pseudpellagra has been a source of much confusion in the literature of this subject, and by some it has been considered a haven of refuge for their opponents when hard pressed by the anti-zeists.

Sir Patrick Manson takes a fling at it with the remark, "The disease is pellagra when it fits in with the orthodox theory and when it can be connected in any way with maize, but, when this is not possible, the disease becomes pseudpellagra."

Ceconni, LeFrer, and several other French writers speak of the pellagrous syndrome, and call it the "morbus miseriae." They go so far as to contend that among alcoholics, and in certain cachectic conditions, more particularly among the insane, symptoms may arise so closely simulating pellagra, that such a diagnosis can be reasonably made. In other words, they go so far as to deny that this is a disease *sui generis*.

The tendency to implicate some protozoal or animal parasite was first brought forward by Dr. Louis W. Sambon, lecturer on Tropical Medicine at the Liverpool School of Tropical Medicine, who was detailed for three months in Italy, where he studied pellagra.

Dr. Sambon, by his researches on the sleeping-sickness,

and his tsetse-fly theory, which has since been proved, established his position as a student, whose views were worthy of respectful consideration.

Briefly and without elaboration, the following is Sambon's theory:

Pellagra is not due to maize, either good or bad, because—

(1) It is found in places where maize is neither cultivated nor eaten.

(2) It is absent from many places where maize is the staple food of the population.

(3) It has in many places either decreased or become more prevalent without any change in the food or the people.

(4) Its constant and peculiar distribution does not agree with the very irregular and ever-changing distribution of spoiled maize.

(5) In over a century and a half, since the maize theory was first suggested, no one has been able to prove it.

The belief that the disease has everywhere followed the introduction of corn cultivation is unfounded. Pellagra was first recognized as a specific disease in the beginning of the 18th century, but this does not prove that it was not prevalent long before that time.

On the other hand, Dr. Sambon makes the following postulates to prove that pellagra is a parasitic disease because—

(1) For years the person affected may present some seasonal recurrences, which can only be explained by a parasitic agent with alternating periods of activity and latency.

(2) It shows a constant and characteristic topographic distribution.

(3) It shows a definite seasonal incidence.

(4) Its symptoms, course, duration, morbid anatomy, as well as its theory, are similar to those of parasitic diseases.

(5) Of two places almost contiguous, one may be affected, the other not.

Again, he contends that pellagra is an insect-borne disease because—

(1) It is limited, like malaria, sleeping-sickness, etc., to rural places, and more especially to the vicinity of certain water bodies.

(2) It has a definite seasonal incidence—spring and autumn.

(3) It effects, to a large extent, a certain class of people—the field laborers.

(4) It is not contagious, and neither food nor water can account for its peculiar epidemiology.

(5) Within its endemic centers it affects all ages and frequently whole families.

(6) Outside its endemic centers only adults who have visited the infection areas present the disease, and frequently only one or two members in a family are affected.

His bill of indictment against the *simulium reptans* is based upon the following proof:

(1) *Simulium* is found in the torrents and swift running streams of all pellagra districts.

(2) *Simulium* has the peculiar seasonal distribution of pellagra (spring and autumn).

(3) *Simulium* is found only in rural districts. It is unknown in towns and villages. It does not enter houses.

(4) *Simulium* explains most admirably the peculiar limitation of the disease to field laborers.

(5) *Simulium* is the only blood-sucking insect which the British field commission has found in its visits to numerous pellagrous districts in Italy.

(6) *Simulium reptans*, like *anopheles maculipennis*, has a world-wide distribution and explains the wide distribution of pellagra. It is found wherever pellagra is found.

(7) *Simulium* causes epizoötics in animals in America and in Europe.

(8) Professor Mesnil has found a protozoal organism in *simulium*.

These statements from Sambon are given principally for their historic interest, for he has abandoned the "simulium theory."

This simulium fly belongs to the diptera, or two-winged flies, belonging to the *simuliidæ* family.

The species located in America are the *simulium venustum*, and the *simulium pecarum*, the buffalo gnat. In Italy Sambon found three varieties—*simulium reptans*, *simulium ornatum*, and *simulium pubescans*. The last named were found in the greatest numbers.

While the topographic conditions in many places in the United States are similar to those in Italy, where the *simulium reptans* abounds, this particular variety is not found out of Europe, with the exception of Greenland, according to the authority of Dr. L. O. Howard, chief of the Bureau of Entomology, United States Department of Agriculture.

Dr. W. D. Hunter, of the same department, says, "All the information at hand seems to show that in this country

there is no apparent connection between pellagra and *simulium*. The centers where *simulium* is most abundant are along the Mississippi Valley, from Baton Rouge north to about Cairo, Ill., and in New Hampshire, Maine, and New York.

"From *a priori* considerations, if there is anything in the *simulium* theory, the centers of pellagrous infection in the United States should be in the localities mentioned rather than in the Southeastern States."

Sambon's ideas, also, that pellagra is nearly always linked to a running stream are not proved by the experience and inquiries of the writer. Out of over 100 cases, where this phase of the probable exposure was carefully gone into, in only 15 was this environment positively brought out. Many were city dwellers, who had not been near streams at all; others had been raised in high and dry localities, and had never to their knowledge been bitten by "sand flies."

The writer must confess that an original favorable conception of the "Sambon theory" has diminished in proportion as he has honestly endeavored to demonstrate its truth, until now he is unable to subscribe to it.

That pellagra appears in those who have "never eaten corn or corn products" is continually being asserted. We can hardly open the pages of a medical journal without seeing some instance of this sort cited, where, with an iconoclastic air, like the "three tailors of Tooley Street, who *resolved* that the earth was flat," the narrators seem to think the zeistic idea has been relegated to the limbo of discredited theories.

A New Orleans observer has reported a case of pellagra,

which for quite a while seemed that it was going to prove an exception to Lombroso's doctrine. This pellagrin was a married woman, who had been raised in a section of country and in a family where corn was considered suitable food for horses and hogs, but not for people. She and her husband iterated and reiterated the solemn declaration that never in her life had she eaten any corn or any food made from corn, when accidentally the physician learned that she was addicted to the use of corn starch, eating a pound or more each day.

This morbid appetite—amylophagia—is not very uncommon, as may be judged by the fact that recently the writer has known of three cases at the clinic for internal medicine at the Atlanta School of Medicine. They were women—one white and two colored—and they admitted the craving with evident reluctance.

That corn in many forms, as an adulterant and otherwise, enters into many articles of daily consumption is an undoubted fact.

A miller recently described the former custom of adulterating the cheaper grades of flour with "corn hearts," though he claimed the pure food laws had practically put an end to it.

Dr. J. L. Campbell has called attention to the fact that most, if not all, of the inexpensive candies on the market have glucose as their base; also most of the table syrups contain this corn product.

The breakfast cereals, a legion of which are constantly on American tables, contain more or less corn. We are served some food containing corn on our uprisings and our downsittings, so that it behooves no one to lightly say that

he or she has never eaten this grain or anything made from it.

Another theory, which the writer will incorporate in this work, is that brought forward by Dr. G. C. Mizell, that the cause of pellagra may be traced to the ingestion of "semidried edible oils."

The writer does not subscribe to this theory, nor has it as yet received approbation in many quarters, but that the present-day views of pellagra may be adequately reflected in these pages, requires that Dr. Mizell's contentions be accorded a reasonable amount of space.

Admitting the possibility of spoiled maize producing pellagra, he deems it impossible, unless the diet excludes all other food, especially fats. He further opines that the fat responsible for the trouble is linolin, a neutral fat, which is present to some extent in all semidrying and some drying oils.

Lest this gentleman should be misquoted, his exact words will be used in the following paragraphs:

"When linolin is consumed in large quantities it is deposited in the tissues as linolin. When it undergoes oxidation poisonous products are formed. These oxidation products are suspected of producing the disease. This would necessarily mean that the disease is biochemical in nature. The amount of linolin consumed will depend on the percentage present in the oil and the amount of oil eaten. Some of the semidrying oils contain such a small percentage of linolin, it is probable that they would not be deleterious to health. This point needs to be emphasized, as it appears that the quantity consumed is important. . . .

“. . . Keep in mind that the import or production of oil does not mean that the oil is always eaten. Many nations import, and some produce large quantities of oil of this class for commercial purposes. Germany is one of these. Germans are not an oil-consuming people. The chief substitute for animal fat in Germany is a non-drying oil, viz., cocoanut butter, the daily production of which is estimated at one hundred tons. A law requires the use of 10 per cent. of sesame oil in the manufacture of margarine. This amount I do not believe is sufficient to cause disease. It appears that it is necessary to introduce comparatively large amounts of linolin into the body in order to produce pellagra.

“ Below is given a table of the semidrying oils and nativity. Many minor oils are omitted, being less used, and only supplementing the more common:

OIL OF—	NATIVITY.
Cotton seed.....	United States, India, Egypt, China, Russia, Brazil, Mexico, Japan, Turkey, etc.
Sesame seed.....	The Levant, India, Egypt, Java, Siam, Algeria, East and West Coast of Africa, South Rhodesia.
Maize.....	United States, Argentina, etc.
Beechnut.....	Manufactured in Europe in 1713, but not at present.
Pinot.....	Brazil and Guiana.
Kapok.....	East and West Indies, South America, Mexico, Africa.
Brazil nut.....	South America.
Luffa seed.....	East India.
Rape seed.....	India, Northern France.
Pumpkin seed.....	Austria, Hungary, Russia.
Sunflower seed.....	Hungary, India, China, South and Southwest Russia.
Poppy seed.....	Asia Minor, Persia, India, Egypt, South Russia, Northern France.

“ Poppy-seed oil is a drying oil, but contains a large percentage of linolin, and is an edible oil of extensive use.

Some of the above oils contain a low percentage of linolin and may be of no importance as an etiologic factor.

" Laws regulating the importation of seed oils into some olive-growing countries have in recent years been enacted, so as to protect the home industry. Some countries growing enormous quantities of oleaginous seed export the seed, and consume very little or none of the oil. Such is the case in China and Japan.

" The people of Southern Europe are noted oil consumers. Italy is the second largest olive-oil-producing country in the world. Notwithstanding the enormous quantity of olive oil produced, much oil is imported. They are also the largest exporters of comestible oils in this region.

" Large amounts of semidrying oils are imported. These are used at home, and exported as edible oils under various labels, and used to adulterate olive oil. These semidrying oils are cheaper than olive oil, hence are consumed by the poor. Cotton-seed oil was probably imported from Marseilles long before it was thought of in America. At the present time it is well known in the Italian market.

" In recent years the demand has increased. It is stated that, when cultivation of lupines was introduced into certain regions, enabling the farming class to raise stock and dispense with maize as a food, pellagra disappeared. It is probable that, instead of pellagra disappearing for the above-named reason, it was in reality due to a change from vegetable oil to animal fat consumption. . . .

" My conclusion from investigation of the seed-oil indus-

try is that since 1817, when the first seed-crushing mill was put into operation in Marseilles, there has been an almost unlimited supply of seed oils. The habits of the various nations and individuals have alone operated in determining the extent of oil consumption. Often the need of cheap food has determined the selection. Until the mills began crushing seed there was no pellagra in France. The peasantry were afflicted because the poor bought cheap food. In the United States the selection of edible fat was not determined by price until the cost of provisions increased about 1908. Until this date, purity of food was the determining factor to a great extent. It is true that the manufacturers have appealed to patronage from both standpoints. They made a cheap article for the poor and a high-priced article for those in better circumstances. Dyspeptics have been shown that the oil is more digestible. The fastidious are told that the oil is pure vegetable oil, clean, and highly nutritious. The Pure Food and Drugs Act is stamped upon each package as a guarantee of purity and wholesomeness. The unsuspecting public, depending upon the guardianship of the government stamp, has adopted cotton-seed oil as a regular article of diet. Various cooking substances, without a single indication of their nature, are coming into the market without even the distributing agent being able (or willing) to name the contents of the package. People are consuming these preparations without question because the government stamp is upon them. This being the case in our own country, who will doubt that the cheap comestible oils shipped (even as pure olive oil) into oil-consuming communities are made up largely of semidrying oil?

"Note the progress of pellagra in the United States. It started in the South, where oil consumption began, and only after it began. Illinois should be placed with the South, both as to oil consumption and pellagra. More pellagra has appeared in California than any other western state. It is significant that she also consumes more cotton-seed oil. A map of cotton-seed oil consumption in the United States would serve as a map showing the geographic distribution of pellagra, except as affected by climate. Nations that have remained consumers of non-drying oils are not afflicted with pellagra. Some of them have eaten maize, just as the inhabitants of the United States have for several centuries, without having developed pellagra. . . .

"Experiments upon animals indicate that pellagra may be caused by eating less than one ounce of oil daily. If this is true, oil may be consumed for medicinal purposes in sufficient quantity to produce the disease, and olive oil should not be administered, unless of known quality."

This is a brief attempt to give the salient features of Dr. Mizell's theories, which, after three years, are still unproved.

The conscientious narrator must admit that the cause of pellagra is still to a great extent an unsolved problem. The zeist doctrine is, on the present state of science, insusceptible of direct proof or direct disproof. There are many reasons why it cannot be disproved. It is impossible to show that any person whose food partook of corn products ate only healthy corn. If the corn was originally healthy it might have been badly kept, or, if well kept, it might have been poorly treated after being ground into meal; or even the meal might have been wholesome, but the

bread or other articles of food made from it might have been allowed to become spoiled, or contaminated by contiguous agencies. So, when one has at any time eaten corn products, there is a chance that it was not absolutely sound.

The idea advanced some time back by the antizeists that pellagra was a "disease of poverty" has been exploded, though at present Dr. Goldberger is arguing somewhat along that line. The many cases in persons of wealth and refinement, where environmental conditions were all that could be wished, have effectually put an end to that chimera. The more positive doctrines, as collated by the late W. Bayard Cutting, Jr., may be enumerated as follows:

- (1) That which attributes pellagra to corn itself, not to spoiled corn. This explanation is inadequate. If corn is lacking in certain nutritive qualities—in gluten, in nitrogenous matter—so is rice, which, nevertheless, does not produce pellagra. (The nutritive qualities of corn have already been favorably considered.) If corn contains a poison, how can so many nations consume it with impunity?
- (2) That which admits spoiled corn as the cause, but thinks that the poison enters not as a toxin ready made, but as a bacterium (*bacterium maidis*).
- (3) Those which attribute the poison to other agencies than the *penicillia*—to the *aspergilli*, for instance, or to the *bacterium maidis*, or to a combination of these micro-organisms.
- (4) Those which, while admitting the direct poisoning from corn as one cause of pellagra, attach considerable importance to other elements—heredity, for instance, or the consumption of alcoholic liquors made from corn.

As far as Italy is concerned, they admit that the consumption of corn, and especially spoiled corn, is at the root of the disease, and official measures including this hypothesis are in motion, which will be covered later under the head of prophylaxis.

Among predisposing etiologic factors poverty, no doubt, plays an important rôle.

That unhygienic homes and surroundings, that ignorance begotten of poverty, and continued by reason of poverty, may dwarf both the body and the intellect, impairing the normal resistance faculty, and making the body a more inviting host for the powers of disease; that cheap, often synonomous with adulterated, food should impair the digestive powers, laying foundations for various stomach and intestinal ills—all these can serve as undoubted factors for the development of pellagra as well as any other toxic or infectious disorder. This has been conclusively shown by the studies of the Thompson-McFadden Commission, whose labors will later receive extended comment. Let them be quoted as follows:

"Another feature of our field work in 1913 has been the survey of communities offering marked contrast in certain particulars. All the mill villages of Spartanburg County were found to be endemic centers of pellagra. All these villages have been using unscreened surface or pail privies for the disposal of human excrement. A careful survey of two other mill villages, one in Oconee County and the other in Chester County, S. C., failed to disclose any case of pellagra which had certainly originated in these villages, although cases which had originated elsewhere were present. In these villages every house was provided with a water-

carriage flush closet connected with a sewer, and this seemed to be their most important distinguishing characteristic. In the city of Spartanburg, S. C., the active foci of the disease were confined to those sections of the city in which unscreened surface or pail privies were in use. Of the 241 cases in the city of Spartanburg itself, for which data on disposal of sewage were available, it was found that 230 were using unscreened surface or pail privies. In only 11 instances, or 5 per cent. of the total, was a water-carriage system of disposal employed, and several of these cases arose in sections of the city where unscreened surface privies were in use by their neighbors, some of whom were pellagrins. In certain hospitals for the insane we have ascertained that pellagra is usually most prevalent and persistent in the wards housing untidy patients."

Apart from these considerations, however, poverty yields no specific influence.

That heredity is a predisposing factor seems fairly well proved. The writer has records of 81 instances where pellagra was observed in the second or third generation; and at present has under observation 28 cases where pellagra has occurred (mostly fatally) in the parents or grandparents.

One instance, where an infant was born of a pellagrous mother, was reported. It seemed that conception took place during a remission of the disease, but the confinement came on during the recrudescence. The infant lived only two months, never thrived, and its skin was harsh and dry during the whole of its brief life.

The mother was treated a short time for the disease, but, after a period of improvement, ceased to report, and the final outcome of her illness was unknown.

The children of pellagrins also seem to fall an easy prey to other diseases, notably those ailments of the alimentary tract. At the clinic for gastro-intestinal disease at the Atlanta School of Medicine hardly a week passes but what some patient reports pellagra in one of the parents.

In regard to race some interesting features have been observed. The Caucasian race seems more subject to it than the yellow or red race. Among the white race, also, the writer has noticed a preponderance among the blondes, perhaps because of their being more vulnerable to the sun's rays.

Dr. Babcock's statement that in the South the disease is more common among the negroes than the whites has not been verified by the writer. That, when among the negroes, it more frequently attacks the women may be admitted, but, among several hundred observed during the last three years, the African race furnished only a small percentage.

Dr. Bernard Wolff, of Atlanta, has adduced the novel theory that the Jews are practically exempt from pellagra. This brings up indirectly the question of heredity, for the Jewish blood is probably more free from admixture with other races than any other. Dr. Wolff has been able to locate only four pellagrins among this race, and the writer has never seen one.

Sex is not supposed to exert any special influence, though about 65 per cent. of the cases coming under our observation have been females. This has not been the experience of others. It would appear that the nervous cases have largely been females.

Habits act on the principles of lessened resistance. Several alcoholics, and, strange to say, those who preferred corn whisky, have been under observations with uniformly fatal results.

One of the most fulminant cases the writer has ever seen occurred in a brawny mountaineer, who, as he expressed it, was "a dear lover of corn liquor," and who lived only about three weeks after the pellagra was noticeably developed.

Venereal excesses, mental strain, pregnancy, and frequent child-bearing all act in the same way—no special predisposition, but lessened resistance.

With few exceptions it does not attack the very young. Most writers claim that infants do not suffer with pellagra unless they are fed on spoiled corn products, and in this the writer agrees.

No cases under five years of age have been personally known, and very few under ten. This malady seems to attack by preference those between the ages of twenty and forty—ages when they can be most useful to themselves, their families, and the community at large. When it attacks those over fifty, the duration is either short or a condition of dementia supervenes.

Occupation was thought at one time to possess a large influence, but this idea is weakening at present. In Italy it has, of course, attacked the rural and agricultural population, as has been proved time and again. In America, however, and especially in the South, occupation has shown but scant influence.

At present the writer has under observation several pellagrins, who are in easy, almost affluent circumstances.

One, an unmarried lady of about forty from an adjoining state, has been in her community a leader in civic reforms, an exemplar in hygiene, a stickler for correct manners of living.

Another is a young woman, the petted darling of wealthy parents, whose every wish was always gratified, and whose surroundings carried every comfort that money could buy.

Along with these cases come farm laborers, horny-handed, with the tan of sun and weather on their faces; operatives in cotton mills, pallid, with flat chests and anemic complexions; dusky-hued sons and daughters of Africa—all suffering from the same dread pellagra.

The spring season certainly has an influence in bringing out the latent symptoms of this disease. How much actual influence the heat and sun have on indirectly causing it by increasing parasitic growths, and hastening the putrefaction of poorly-kept food products, is only a matter of conjecture. That the actinic rays of the sun are instrumental in producing the erythema cannot be gainsaid. Furthermore, after the erythema is apparently healed, the sun, or even bright light, can bring it back again, is the experience of the writer and many others.

Certain it is that pellagra is a disease of summer and warm weather, and that spring and summer exert a deleterious effect, while cold weather is beneficial, is known to all who have had any experience with it.

It has been claimed in Italy that humidity exerted a predisposing influence, and that the disease was more rife after a wet summer than a dry one. Such has not been noted in the United States, nor in the South, though the few years of our observation here are not sufficient for an intelligent opinion on this score.

Probably the most scientific and painstaking series of investigations as to the etiology of pellagra have been furnished by the Thompson-McFadden Pellagra Commission, a body of laborers made possible by the munificence of Col. Robert M. Thompson, of New York City, and Mr. J. H. McFadden, of Philadelphia. The funds thus supplied supported a research expedition for the study of pellagra in the United States, the members of the body being one designated by the Surgeon-General of the Army, one by the Surgeon-General of the Navy, and one by the authorities of the New York Post-Graduate Medical School. The commission was constituted as follows: Captain J. F. Siler, Medical Corps, U. S. Army, representing the Medical Corps of the U. S. Army; Passed-Assistant Surgeon P. E. Garrison, U. S. Navy, representing the Medical Corps of the U. S. Navy, and Dr. W. J. McNeal, Professor of Bacteriology and Pathology, New York Post-Graduate Medical School, representing that institution. In the spring of 1912 the Bureau of Entomology of the U. S. Department of Agriculture detailed Messrs. A. H. Jennings and W. V. King to aid the commission by investigating the possible etiologic relation between insects and pellagra.

A field headquarters was established in the South early in June, 1912, and, in collaboration, biologic, pathologic, and chemic studies were undertaken in the laboratories of bacteriology, pathology, and pathologic chemistry of the New York Post-Graduate Medical School under the supervision of Dr. Jonathan Wright, Director of Laboratories, and Dr. W. J. McNeal, a member of the commission. Other researches along these lines were carried out by Drs. O. S. Hillman, R. M. Taylor, V. C. Myers, and M. S. Fine.

For reasons considered sufficient, Spartanburg, S. C., and the county of the same name were made field headquarters, and the disease was there studied most intensively. The epidemiologic investigations have led to the accumulation of a very large mass of data concerning the occurrence and distribution of pellagra in Spartanburg County and city, in regard to the cases themselves and their conditions in life.

As a fitting corollary to the field work was laboratory work in New York, which was accomplished by sending patients suffering from this disease from the field headquarters in South Carolina to the Post-Graduate Hospital in New York City.

It would be impracticable to include all of the interesting data furnished by these painstaking and conscientious gentlemen, but the several conclusions will be given.

Summary of first "Progress Report" covering work of 1913:

"(1) The supposition that the ingestion of good or spoiled maize is the essential cause of pellagra is not supported by our study.

"(2) Pellagra is, in all probability, a specific infectious disease communicable from person to person by means at present unknown.

"(3) We have discovered no evidence incriminating flies of the genus *Simulium* in the causation of pellagra, except their universal distribution throughout the area studied. If it is distributed by a blood-sucking insect, *Stomoxys calcitrans* would appear to be the most probable carrier.

"(4) We are inclined to regard intimate association in the household and the contamination of food with the excretion of pellagrins as possible modes of distribution of the disease.

"(5) No specific cause of pellagra has been recognized."

In the last report of this Commission, published in the Archives of Internal Medicine, January, 1915, a number of later conclusions are adduced.

A synopsis of their statistics as to age of pellagrins is as follows: "Pellagra was absent or very rare in children under two years of age, only very slightly prevalent for the five years following puberty in both sexes, and only slightly prevalent in adult males under fifty years of age. On the other hand, it was enormously prevalent and severe in females from twenty to forty years of age, somewhat less prevalent and nearly always mild in children of both sexes from two to ten years of age, and almost equally prevalent in old people of both sexes. These features of the age and sex distribution are believed to be due in part to differences in physiological resistance to pellagra and in part to differences in frequency and extent of exposure to the disease, especially by proximity to or association with other pellagrins."

Summary of last report:

"(1) The geographical distribution of pellagra in Spartanburg County, S. C., has been uneven, the morbidity being much higher in and near the large centers of population and especially in the cotton-mill villages.

"(2) Pellagra was found to be about three times more prevalent in the white race than in the negro population of this county. This ratio is not regarded as a true measure of the relative racial resistance to the disease, but rather as the end-result of the influence of several factors.

"(3) The substance of this paragraph in report has been given in synopsis above.

"(4) The peculiarities of age and sex distribution are believed to be due in part to differences in physiological resistance to the disease, and in part to differences in degree and frequency of exposure to the causative factors, among which proximity to or association with pellagrins seems to be important.

"(5) No direct relation of occupation to pellagra morbidity was discovered. Indirectly, by determining economic status and environment, occupation was found to have an important bearing on the prevalence of the disease."

Up to the present the individual members of the Commission have not committed themselves to any statement as to the etiology of pellagra, though Dr. J. F. Siler, in a carefully worded communication, writes: "We feel that when all the information which we have collected has been brought together and analyzed, that it will indicate very strongly from the epidemiological standpoint that pellagra is a low-grade infection of some kind. We are inclined to believe that the primary lesions occur in the intestinal canal. We also feel very strongly that it is necessary that predisposing factors be considered in the etiology of pellagra, and one of the most important predisposing factors is diet (and nutrition). We do feel, however, that it is not possible to explain pellagra from the viewpoint of a deficient diet alone."

Pellagra and Potable Waters.—In a recent monograph of nearly 200 pages Alessandrini and Scala have presented a series of epidemiologic studies on pellagra, which led them to regard the disease as etiologically related to potable waters used in pellagrous sections.

Their experimental work was conducted on guinea-pigs, rabbits, dogs, and monkeys. It consisted in the injection

and ingestion of colloidal solutions and gelatinous suspensions made from the potable waters; along with numerous variations in the diet of the animals, especially with reference to a diet of maize. In some experiments they made additions to their solutions of certain salts, notably of calcium, sodium, and aluminum, for the purpose of testing the action of certain electrolytes on the colloidal silica or of the contemporaneous action of the two (that is, colloidal silica and electrolytes) on the organism.

In an analysis and discussion of results the authors express the conviction that they have produced in their animals a chronic intoxication which not alone in essential features but even in details closely approximate pellagra as seen in man. This they assert is true not only of clinical phenomena, but also of morbid pathologic changes.

This is their condensed argument: "Colloidal silica displays more or less affinity for mineral salts, and from metabolic studies on dogs under experiment, without doubt, silica in the animal organism acts by accumulating mineral substances, and produces in consequence a destruction of tissues. Therefore it seems to us, without doubt, that the silica fixes the mineral salts on the proteins of the tissues with a continuous, incessant action quite similar to the action of an enzyme or diastase." Continuing, they opine that "conditions exist in the formation of these compounds of protein substances with mineral salts by which the acids of such salts are liberated, because there is a tendency in said compounds to pass from the state of metallo-acido-protein to that of metallo-protein."

By further argument, analysis, and experimentation they arrive at their final conclusion that "pellagra is a malady

caused by the forced retention of mineral salts, which, in turn, produces a liberation of acids in excess of the needs of the peculiar organism; or, in other words, pellagra is nothing more than a mineral acidosis with all of its consequences."

The writer has no special comment on these ingenuous arguments, simply including them to "make the record complete."

Elsewhere in this volume mention is made of the fact that at no time under the observation of the writer has a nurse or attendant of one or many cases of pellagra developed the disease.

In a recent article (Reprint No. 203, Public Health Reports) Dr. Joseph Goldberger, Surgeon U. S. Public Health Service in Charge of Pellagra Investigations, remarks: "In considering the significance of various institutional reports, it is to be recalled that at all of these institutions the ward personnel, nurses, and attendants spend a considerable proportion of the twenty-four hours, on day or night duty, in close association with the inmates; indeed, at many of these institutions, for lack of a separate building or special residence for the nurses, these live right in the ward with and of necessity under exactly the same conditions as the inmates.

"It is striking, therefore, that although many inmates develop pellagra after varying periods of institutional residence, some even after ten to twenty years of institutional life, and, therefore, it seems permissible to infer, as the result of the operation within the institution of the exciting cause or causes, yet nurses in attendance living under identical conditions appear uniformly to be immune. If pellagra is

a communicable disease, why should there be exemption of the nurses and attendants?"

Dr. Goldberger has given the etiology of pellagra careful study, and his theories are worthy of consideration. They will be given verbatim:

"The explanation of the peculiar exemption under discussion will be found in the opinion of the writer in a difference in the diet of the two groups of residents. At some of the institutions there is a manifest difference in this regard; in others none is apparent.

"The latter would seem to be a fatal objection to this explanation, but a moment's consideration will show that such is not necessarily the case. The writer from personal observation has found that, although the nurses and attendants may apparently receive the same food, there is, nevertheless, a difference, in that the nurses have the privilege—which they exercise—of selecting the best and the greatest variety for themselves. Moreover, it must not be overlooked that nurses and attendants have opportunities for supplementing their institutional dietary that the inmates, as a rule, have not.

"In this connection brief reference must be made to two other epidemiological features of pellagra. It is universally agreed (1) that this disease is essentially rural, and (2) associated with poverty. Now there is plenty of poverty and all its concomitants in all cities, and the question naturally arises why its greater predilection for rural poverty? What important difference is there between the elements of poverty in our slums and those of poverty in rural dwellers? It is not the writer's intention to enter at this time into a detailed discussion of these questions; he wishes to point

out one difference only. The difference relates to the dietary. Studies of urban and rural dietaries have shown that, on the whole, the very poor of cities have a more varied diet than the poor in rural sections.

"With regard to the question of just what in the dietary is responsible, the writer has no opinion to express. From a study of certain institutional dietaries, however, he has gained the impression that vegetables and cereals form a much greater proportion in them than they do in the dietaries of well-to-do people; that is, people who are not, as a class, subject to pellagra.

"The writer is satisfied that the consumption of corn or corn products is not essential to the production of pellagra, but this does not mean that corn, the best of corn, or corn products, however nutritious and however high in caloric value they may be, are not objectionable when forming of themselves or in combination with other cereals and with vegetables a large part of the diet of the individual.

"In view of the great uncertainty that exists as to the true cause of pellagra, it may not be amiss to suggest that pending the final solution of this problem it may be well to attempt to prevent the disease by improving the dietary of those among whom it seems most prevalent. In this direction I would urge the reduction in cereals, vegetables, and canned foods that enter to so large an extent into the dietary of many of the people in the South, and an increase in the fresh animal food component, such as fresh meat, eggs, and milk."

The etiology of pellagra is yet unproved, though the reader should remember that the time is not yet ripe to cast aside as worthless the tomes of written evidence gathered through

nearly two centuries by Italian and French investigators, and now being augmented by scores of able research workers on both sides of the water.

The writer has not cast to the winds the "Zeist" theory, though agreeing in the main with the conclusions of Dr. Goldberger. He has endeavored, however, to give every side of the vexed question, permitting the reader to form his own conclusions.

Lombroso said: "*In pellagra, then, we are dealing with an intoxication produced by poisons developed in spoiled corn through the action of certain micro-organisms in themselves harmless to man.*"

If to Lombroso's dictum of spoiled corn we add *spoiled carbohydrates*, the statement will come near embracing our latest and most reasonable theories as to the causation of pellagra.

CHAPTER IV

SYMPTOMATOLOGY AND CLINICAL COURSE OF PELLAGRA

SELDOM in the history of diseased processes has there been studied one whose symptoms and clinical history presented such a varied panorama as pellagra.

Its many characteristics have placed it in quite a number of categories covered by specialties in the different fields of medical endeavor. The gastro-enterologists have dwelt on the ever-present digestive disturbances, often the first noticeable manifestations of illness, the anorexia, the epigastric discomfort, the diarrhea, and all that train of gastro-intestinal ills.

The dermatologists have noted the skin lesions, beginning with the simple erythema, and developing the various grades of dermal inflammation. Their contention has had the weight of "external evidence," for few cases of pellagra have there been who did not at some stage show an eruption of some sort.

The neurologists and alienists have found in pellagra a fertile field for research and discussion. The nervous and mental symptoms cover a range extending from undefined irritability and change of disposition to dementia or acute mania; exhibiting abnormalities resulting from simple lack of poise up to organic nerve degenerations of fatal proportions.

The surgeons, too, have figured in pellagra, for transfusion of blood from healed pellagrins or healthy donors has excited wide comment, and at one time seemed to promise a therapeutic solution. Even cecostomy and appendicostomy have been advocated for the toxemia, though few pellagrins have consented to such an ordeal, seeming to prefer the ills they have rather than fly to those they know not of.

To attempt to follow the course of pellagra from one viewpoint, or to permit it to be narrowly classed as a manifestation of one organ or set of organs, would be erroneous. It would be unjust to the patient, unfair to the honest student, and productive of endless confusion.

In addition, pellagra does not always appear in the same form. There are variations, brought about by age, race, occupation, previous state of health, previous habits, environment, heredity, diet, recurrence of the disease, and a host of other modifying circumstances, that have to be taken into account in making up an estimate of the true nature and progress of this malady.

Again, there are other features which must not be taken into account in the clinical study, as types, being classified by Lombroso as the cerebral, the gastric, the florid and others—some of these classes appearing rather unscientific for such an authority. The division, as suggested by some, into herpetic or erythematous, nervous or digestive, may be set aside as misleading, because these symptoms may appear, and frequently do, simultaneously.

The elder Strambio, to whom reference has been made, divided pellagra into three types—the intermittent, or that appearing at intervals, between which the patient



Typic pellagrous erythema of hands and wrists. (Courtesy of Dr. J. J. Watson, Columbia, S. C.)

seemed perfectly well; the remittent, in which the disease was better at certain seasons, though not entirely well; and the continuous, where no improvement took place at any time, but the illness progressed uninterruptedly to a fatal issue.

In Italy, among the rural population, there are seven kinds commonly spoken of: (1) Those who go mad; (2) those who are drawn to water; (3) those who go backward; (4) those who are doubled up; (5) those who become giddy; (6) those who are always hungry; (7) those whose skin peels.

Roussel, the most renowned French authority, has to an extent followed Strambio's classification, only he has made out a more logical case. His division is in three degrees primarily, and several others secondarily.

His pellagra of the first degree corresponds to the intermittent form of Strambio, only he subdivides this into *commencing pellagra* and *confirmed pellagra*.

His second degree, he calls *paralytic pellagra*, conforming to the remittent form of Strambio.

Roussel's third degree is denominated *pellagrous cachexia*, subdivided into that with the eruption, or a form without any eruption, being his idea of a pseudopellagra, or a cachexia dependent upon some degenerative or somatic stigmata.

The division, as made by some, into commencing or confirmed pellagra, is certainly not a practical one clinically, for some, for instance, inveterate alcoholics, may be beyond successful treatment from the very first appearance of the disease; while other pellagrins assume a state of extreme chronicity, never becoming seriously ill with the pellagra,

and always apparently amenable for a time to favorable hygienic surroundings or proper medicinal treatment.

It would appear to the writer that a classification, somewhat like that of Babes and Sion, is preferable, though even their classification cannot be followed in its entirety.

They recognize a (1) prodromal stage, or pre-erythematous; (2) a stage in which there are erythema, more or less gastro-intestinal disturbances, and vague symptoms of peripheral nervous disquietude; (3) a stage of deep depression, bodily and mental, with accompanying cachexia.

The simplest classification would naturally be the best, if it were possible to adopt such. The fact is patent, however, that the evolution of pellagra from one stage to another cannot always be followed; that the original manifestations may be either cutaneous, gastro-intestinal, or nervous, or even pscyhic; that, while ordinarily pellagra is a chronic affection, there are some fulminant cases, where no line of demarcation can be noted from stage to stage; and that the cachexia may come on early or late, according to the patient's power of resistance.

As emphasized by Dr. Babcock, it is well to recognize from the start that pellagra is a trophoneurosis. Neurasthenic symptoms, though vague and nebulous, are often the first noticeable changes, and, when seen with the clearer eye of retrospection, are often as plain as the noonday sun.

It should be remembered that the types vary in different families or individuals. That it varies in races, or those peoples situated far apart, has already been allowed.

In some the gastro-intestinal symptoms predominate,

the patient having probably inherited poor digestive powers; in others, where an unstable nervous system, made more unstable, perhaps, by faulty habits, predisposes to nervous manifestations, such may predominate, masking every other feature.

That seasonal influence may affect the skin, or that some cases may be apparently confined to cutaneous lesions alone, has been observed.

At present the writer has under treatment a young girl of sixteen, who has undoubtedly the erythema of pellagra, and yet has never had a single qualm of any other bodily disturbance produced by her ailment, and she claims to be not the least ill.

Sandwith does not subscribe to a "prodromal period," but considers pellagra to have an incubative period of nine to twelve months' duration, in which time there are undefined feelings of ill-being.

To all intents and purposes, however, the writer thinks it well to admit the existence of a real prodromal period, during which the incipient pellagrin complains of malaise, languor, neuralgias, indefinite pains, anorexia, occasional "digestive upsets," and an indescribable sense that all is not well.

This may last for several years, may never develop into pellagra, or may merge into a typical case. One can never tell.

Dr. H. F. Harris goes so far as to say that a majority of the people of the South to-day are suffering from one form or another of "corn-bread poison," as he terms it; that numberless cases of indigestion that eventually recover; that many unrecognized cachexias eventually clearing up;

that hundreds of so-called auto-intoxications are in reality manifestations of "corn-bread poison."

This extreme view may not be accepted in its entirety, but there is more than a modicum of truth in his assertion. This he has proved in some instances by the quick gain in health after all corn products have been eliminated from the dietaries of some of these sufferers from obscure complaints.

Parenthetically, in this connection, it might be well to caution the reader to be on the *qui vive* in all cases of atypical digestive disturbances, lest later on pellagrous symptoms supervene, to the chagrin of the medical attendant.

Another source of error abides in those who have for long periods of time suffered with chronic indigestion, either functional or organic. During this long-drawn-out time these individuals have become so accustomed to their epigastric and abdominal discomforts that they ascribe all their ills to the "old case of indigestion," and fail to recognize the advent of a new factor in the pathologic drama.

The writer has records of pellagrins with concurrent chronic gastritis of long standing, of obstinate hyperchlorhydria, of gastric and duodenal ulcer, of achylia gastrica (quite frequent), of cholangitis and cholecystitis, of confirmed constipation with its train of accompanying toxemias, and a few have been, as they say, "life-long dyspeptics."

Gastric Symptoms.—The gastric symptoms of pellagra do not differ materially from those of chronic catarrhal gastritis, mostly of the hypo- or anacid variety. In gastric

analyses of 64 cases of undoubtedly pellagra, free hydrochlorid acid was absent in 18, deficient in 31, excessive in 12, and normal in 3. There was an excess of stomach mucus in 41 of these. In those who were nauseated, or suffered from frequent vomiting, bile was found in the stomachs of nearly every one. The test for occult blood was positive in 4. It was particularly noted that the gastric secretions were diminished or absent in most of the cases of long standing, and a few, where those juices were increased, were rather recent cases of pellagra.

Roussel considered the anorexia, nausea, and gastric indigestion as only complications, while he thought dryness of the esophagus, with dysphagia and pyrosis, the first true pellagrous symptoms. This fine-cut distinction would be hard to put in practice.

Frequently the first train of ailments that brings up a suspicion of pellagra is a sensation of burning in the mouth and stomach, accompanied by vague neurasthenic fancies. Slight paresthesias and formications of small areas are generally also present. Upon examination, the physician observes a diffuse redness of the buccal mucosa, sometimes with a few aphthous spots. This redness is not the bright scarlet of scarlatina, nor is it the angry hue of stomatitis proper, but rather a decided pink, glistening on the mucous membrane and imparting to the lips a cherry red, with a well-marked line of demarcation at the junction of the skin.

This buccal redness may increase, merging into vesicles or even superficial ulceration. Aphthous spots, about the mouth and on the tongue, are quite common, especially on the tip of the tongue and in the different sulci behind

the gums and near the fauces. Where plates of artificial teeth are worn, the surfaces where the plates come in contact are nearly always sore and ulcerated.

Another point which has not been dwelt on is the tendency for the corners of the mouth to become sore. Numbers of sore mouths have been treated by the writer, where, after all the other lesions were healed, the corners still remained raw and irritated.

During this period of stomatitis and glossitis the salivary glands are quite active, even to the point of the saliva flowing involuntarily from the mouth. Some observers have claimed the saliva was acid, but, if so, it has not been present in any of the cases seen by the writer. Procopiu does not think this excessive secretion of saliva, amounting to ptyalism, is caused by the buccal irritation, but by the action of the toxins upon the salivary glands or the central nervous system.

The appearance of the tongue in pellagra is often quite characteristic. It may be coated centrally, but the edges are smooth and slick, showing a surface denuded of epithelium. The papillæ, while pronounced and sometimes injected, show no special diagnostic points. In recent cases only the extreme tip and sides show this denuded condition, but later on the whole tongue may lose its epithelium, giving it a peculiarly bald look, sometimes called the "cardinal tongue." When the redness is pronounced the tongue may be exquisitely sensitive and sore, but often a semipallor follows the loss of the epithelium, and a lack of feeling almost akin to anesthesia supervenes.

So often has the writer heard expressions of self-con-

gratulation over supposed improvement of a sore tongue, when it was only the temporary anesthesia that would be followed by a greater soreness.

This peculiar but almost constant sore tongue seems plain enough now, since the medical profession are on the lookout for pellagra, but in the years gone by gave rise to various and sundry diagnoses that would seem ridiculous, had they not been fraught with such possible serious consequences to the bewildered sufferers.

"Superficial glossitis," "chronic glossitis," "Egyptian scurvy," "sprue," "tobacco tongue," and a host of other sobriquets settled nothing, and kept both the patient and physician floundering in the shallows and breakers of uncertainty.

In recalling some obstinate sore mouths of former days, the writer is confident that a generous percentage, though attributed to "spoiled stomachs," to auto-intoxication, to chewing strong tobacco, and other causes too numerous to mention, were in reality the manifestations of pellagra that never fully materialized.

At this early stage pellagrins often complain of shooting pains, almost equal to the lightning pains of tabes. Several instances of this sort have occurred, where incipient locomotor ataxia was more than suspected, only to develop into pellagra later on.

We are informed that in the European countries April and May are the months in which the more positive symptoms make their appearance. This is true, to a marked extent, in America also, but May and June seem to bring out the pellagrous manifestations rather more than any other months. Dr. Babcock's opinion that September

and October are unfavorable months has not been verified by the writer. October, instead of being a hard month on pellagra, often ushers in the first improvement; probably on account of the beginning of cool weather.

Skin Symptoms.—The dermal manifestations will be next considered, though let it not be understood that they are necessarily the first; on the contrary, they sometimes do not appear until late in the course of the malady, and in exceptional instances accompany the closing scene.

The first eruption begins as an erythema, not unlike a sunburn, and, as it generally shows on the exposed parts of the body, is often attributed to that agent. This erythema usually begins in the spring months, because, it is thought, the actinic rays of the sun are then specially strong.

Though this skin lesion gave pellagra its name, it should be no more considered a purely skin disease than leprosy or syphilis.

This erythema, when first noticed, consists of a redness, swelling, and tension of the skin, which sometimes persists only a short time, leaving the surface where it appeared scaly and rough.

One of the most characteristic features of the eruption is its symmetry. A skin lesion seen on one hand or arm is almost sure to be duplicated on the other hand or arm; or one showing on one side of the face or one part of the body is equally seen on the corresponding side or part. This has become so well recognized as a diagnostic factor that any one of experience, who sees a "one-sided" eruption, would require much corroborative evidence of other kinds to make out a diagnosis of pellagra.



Typic pellagrous erythema of hands. (Courtesy of Dr. J. J. Watson,
Columbia, S. C.)



Showing scaling epidermis after erythema and vesication. Note absence
of ulceration of newly formed skin. (Case from Peoria State Hospital.)

Many have been the cases diagnosed as *eczema*—that dermal mantle of ignorance, covering so many diagnostic shortcomings. The name *eczema*, having a pseudoscientific sound, and being easily remembered by those whose dermatologic phraseology had become hazy, was generally applied to all sorts of skin eruptions, and little more thought of it until other bodily symptoms forced a more thorough study of the trouble.

As Dr. Watson says, “The only type of eczema worth our consideration is erythematous eczema when it affects the hands or face. In this condition we would not have the tongue or digestive phenomena that occur in pellagra; and while these symptoms may be very mild, a history of their presence can be obtained if the patient is properly questioned. There are many points of difference between the erythema of pellagra and erythematous eczema, but the most important one is the line of demarcation between the erythematous area and healthy skin in pellagra, whereas in erythematous eczema there is no line of demarcation, the erythematous area merging into the healthy skin almost imperceptibly. The itching in eczema is marked, whereas pellagrins, if complaining at all, only refer to the *burning* of the skin lesion; it never itches. Eczema has not the tendency to assume the light chocolate color that is so characteristic of pellagra. In erythematous eczema, as in other forms of eczema, you are very likely to find other eczematous lesions on the body.”

The sharp line of demarcation between inflamed and healthy skin is also ably described by Dr. Howard Fox in a recent paper. He said in part, “A characteristic feature of the skin lesions, fully as important as the symmetry, is

the sharply circumscribed border seen most frequently in the patches upon the neck and hands. Indeed, the lesions upon the neck, forming the so-called "neck band" of Casal, are absolutely distinctive, and could not well be confused with any other lesions of the skin. Several illustrations are seen in Merk's book which are almost perfect counterparts of some cases seen in the South. None of these cases presented sternal prolongation of the neck-band, the so-called 'appendix fascioleæ' of Casal. Most of the cases were, however, in women.

"A striking picture was also presented by the eruption on the backs of the hands and wrists, when the characteristic border was present. In many cases this border was seen not only on the back, but also upon the front of the wrists. In the cases in which the eruption was disappearing, the sharp border was no longer visible."

The writer is glad that Dr. Fox brought out this last point, for the line of demarcation being sharply cut or fading into obscurity often tells the difference between an augmenting or a declining state of pellagrous disease.

To continue with Dr. Fox, "Comparatively few of the cases showed lesions upon the face. In one case there were lesions upon the neck and cheeks, which at first glance looked much like a burn that might have been produced by carbolic acid. Some of the cases presented lesions upon the dorsal surfaces of the feet. In others, the lesions involved the greater part of the legs and resembled an eczema. Few of the lesions noted upon the feet presented a sharply marked border."

Another skin lesion sometimes confounded with pellagra is *erythema multiforme*. To quote Dr. Watson, "Like



Typic cervical involvement, showing well-marked "butterfly." (Case from Peoria State Hospital.)

pellagra, the lesions are symmetric, most frequent upon the extensor surface of the forearms, hands, legs, and feet; not accompanied by marked subjective sensations. It differs from pellagra in that the erythematous lesions are markedly raised and the skin between the various lesions is of normal color."

Dr. Watson mentions six cases treated for poison oak, and the writer recalls several. This error could have been avoided by ascertaining that none of the cases had been where they could have encountered the poisonous plant, and also by remembering that the vesicles first occur between the fingers, and extend from this point, and that in pellagra there are not often seen vesicles, but large bullæ.

Quite an interesting case was some time ago reported to the writer, in which a young man in South Georgia, while convalescing from pellagra, and after the erythema on his arm was nearly faded, came in contact with some poison oak, and had a sharp attack of irritation on his wrists and hands. The poison oak dermatitis was severe and painful, but it did not seem to have the least influence on the pellagrous erythema. After the dermatitis had abated, the vesicles had disappeared, and all itching had ceased the characteristic skin lesion of pellagra was still in evidence, seeming to have not been affected at all.

Another unique case was reported from Florida, where, during an outbreak of smallpox, a lady with a disappearing pellagrous erythema decided to be vaccinated. Her vaccination "took" in short order, and for several days she had an extremely sore arm, the inflamed area from the vaccination being superimposed over the original reddened surface. She also had fever, general aching, and

all the uncomfortable symptoms of a vaccine infection, but the course of the pellagra was not modified in the least. Her bowels, which were inclined to diarrhea, remained the same, and some evidences she showed of a secondary pellagrous neuritis were neither mitigated nor deepened.

Another skin lesion mentioned by Dr. Watson, as sometimes mistaken for pellagra, is *lupus erythematosus*. This might cause some confusion, but only when the pellagrous erythema attacked the face, producing the characteristic lesion across the nose; this, however, is practically impossible without the hands being affected at the same time, which, of course, would at least arouse the suspicion of pellagra, and a search for stigmata of the disease would be made, and, if found, would dispel any doubt that might exist.

Dr. Howard Fox, in his article entitled "Personal Observations on the Skin Symptoms of Pellagra," remarks, "The name erythema, by which the eruption of pellagra is generally denoted, does not appear to me to be entirely appropriate. It would seem quite proper to use the term erythema for the first stages of the disease, which resembles an ordinary sunburn and which lasts only a few days. But it seems somewhat anomalous to speak of the entire eruption as erythema, when the erythematous stage is so comparatively insignificant, while the stage of desquamation is so characteristic and of such long duration. An eruption which is called an erythema conveys the idea of affections such as erythema multiforme or the so-called toxic erythema, which are not, as a rule, accompanied by desquamation. The general term dermatitis would be a more appropriate name, in my opinion, than erythema for



Symmetric erythema and pigmentation in pellagra. (Courtesy of Dr. J. W. Babcock.)

the pellagrous eruption. This dermatitis particularly affects the back of the hands, the lower third of the forearms, occasionally also the dorsum of the feet; it also appears on the face, neck, and upper part of the chest; in fact, on the places that are uncovered and exposed to the sunlight. In the case of persons who, while laboring, go almost naked, such as the fellahs in Egypt, the greater part of the body is affected."

In Roumania, where many children run naked about the streets, the erythema is not confined so much to the locations on the body mentioned, but are much more widely disseminated. Such has also been reported from Rhodesia.

Dr. Babcock, referring to instances in Algiers, France, and also South Carolina, says, "Attention has been directed to a dermatitis occupying the whole vulvar region, as well as the perineal, the anal fold, and the internal surfaces of the thighs, which are brought in contact by adduction. Here pressure, as was noted by Sandwith, is clearly an exciting cause of the inflammatory eruption. In many of our cases the surface of the elbows and, to a less extent, of the knees is involved for a long while. There is also a tendency for the dermatitis to extend from the elbow down the ulnar, sometimes meeting the 'gauntlet' coming up from the hand. Here, again, pressure is a causative factor."

Scheube remarks, "The skin becomes red and swollen, causing the patient to experience a sensation of tension, itching, or burning. Sometimes little blebs and pustules, that dry up to scabs, develop. After the erythema has subsided for a few weeks, a desquamation of the epidermis in large patches takes place."

The vaginal and anal irritation has been frequently seen by the writer, and has constituted a most painful complication in every instance. In some of such cases the bowel evacuations were watery, acrid, and occasionally involuntary, so that the constant flow of this irritating fecal discharge over the inflamed surface gave rise to excruciating agony.

This inflammation of the mucous membrane and margins around the vulva and anus occasionally take on a diphtheritic aspect, edema may occur, followed by bullæ, pustules, and, in rare cases, even by gangrene. Such are sometimes called the "wet cases."

It is probable that some of these cases were diagnosed dermatitis exfoliativa in the United States some years ago.

In pellagrins where the eruption has persisted for a long time it tends to assume a dingy black hue, rough and hard, and exceedingly disagreeable to the sufferer. These dark patches are more often noticed on the palms of the hands, the soles of the feet, on the sides of the nose, or on the forehead, at the junction of the eyebrows.

When the pellagrous eruption begins to abate it first fades by degrees, and, if not too deep, desquamates in fine branny scales, leaving a bright denuded surface, eventually becoming normal. During this time exposure to the sun's rays, or even bright light, may set up a renewal of the erythema.

The deeper forms of pellagrous dermatitis may exfoliate in large scales, leaving raw, bleeding surfaces, or even ulcerated patches, requiring granulations for healing.

The very deep inflammations of the skin, where extensive loss of tissue and gangrene take place, are rare, generally



Symmetric discoloration of both forearms in pellagra. (Case of Dr. G. A. Zeller.)

marking the terminal symptoms, and associated with utter failure of vital resistance.

The skin lesions of pellagra are many and varied, but the writer feels that these descriptions, taken in connection with the illustrations of the different types, should enable the reader to form a satisfactory idea of their appearance.

Digestive Symptoms.—Some of the objective findings of the stomach conditions have been previously touched, but the general digestive disturbances are of the utmost import and deserve careful study.

The views of Babcock, Roussel, Procopiu, and Merk figure largely, correllated with the personal experience of the writer.

One of the first symptoms of pellagra is an undefined dyspepsia, with flatulence, pyrosis, eructations, and epigastralgia. A large majority of pellagrins are dyspeptic, this symptom persisting to a lesser degree during remissions of the disease. This indigestion may remain in evidence for several years, during which time no typical pellagrous symptoms may appear, and this has occasioned Roussel's term "*pellagra sine pellagra*." He said, "The expression *pellagra sine pellagra* can only be applied to a temporary absence of the cutaneous eruption, either at the beginning or during the course of the malady." Strambio also admitted this term, though he stressed the caution that no positive diagnosis of pellagra should be made when there was no eruption, unless there was other decided corroborative evidence.

The epigastralgia is a most common, sometimes perplexing, symptom, coming on at irregular intervals, and apparently bearing no relationship to the amount or kind of

food ingested. This pain has a slight resemblance to the gastric crisis of locomotor ataxia, but should be easily differentiated if proper care is exercised.

The intense burning of the esophagus and stomach, so often in evidence, is seldom due to increased hydrochloric acid, for that, as has been shown, is nearly always diminished. This burning is probably analogous to the burning of the tongue and mouth, and to that in other parts of the body, to be mentioned later.

It should not be forgotten that pellagra can be engrafted on to any of the functional or organic gastric affections, and may complicate the picture, early or late, in the course of the disease.

Periods of anorexia, interspersed with happier periods of normal appetite, even bulimia, are among the early symptoms. It is not uncommon, however, for the patient to suffer with akoria, or the sense of increased satiety, where he feels a craving for food, but finds himself unable to eat but a few mouthfuls before feeling as if an overwhelming meal has been consumed. Occasionally, on account of the epigastralgia, the sufferer fears that different articles of food disagree, until there is developed a sitophobia, or morbid fear of food, which may lead to dangerous inanition unless corrected. This last-named symptom is usually found in cases where nervous or psychic symptoms predominate.

Vomiting is seldom present, and not infrequently patients clamor for solid food when they know full well that they cannot digest nor assimilate it. Records of over 200 cases, searched with regard to vomiting, show it present in less than 20.

Gastric flatulence is extremely frequent, accompanied by loud and explosive eructations. A few patients in the early stages of pellagrous indigestion have been known to acquire the habit of aërophagia, leading to constant and disconcerting eructations, which bore no relation to the food eaten.

The sense of epigastric weight after meals, mainly in those pellagrins with previous gastric catarrhs, is often noted. They complain bitterly of this, sometimes walking partly doubled up in the hope of temporary relief.

The few cases of duodenal ulcer complicating pellagra have shown all the clinical symptoms of that entity plus those of the pellagra. The same may be said concerning the cases of peptic ulcer.

Flatulence is also frequently observed in the small intestine, occasioning abdominal discomfort, borborygmi, and colicky pains. Very often increased peristalsis is set up soon after each meal.

In one instance the writer had the opportunity of examining the duodenal contents of a pellagrin. The contents were obtained by the Einhorn duodenal bucket, which was withdrawn ten hours after swallowing. The contents were a golden yellow, thick and turbid, and showing no reaction for trypsin. This, of course, proves nothing, being mentioned only as a matter of interest.

Occasionally constipation is found in the earlier stages of pellagra, but this is exceptional. The few instances coming under the writer's notice were chronically constipated long before the advent of the pellagra. A case of pellagra, where constipation persists, may be classed as a decided rarity.

The usual rule is to get a history of attacks of diarrhea, apparently causeless, not depending on what is eaten, and ceasing suddenly. This diarrhea is believed by Babes to be due to irritation of the sympathetic ganglia and the plexus of Auerbach. This view has only recently been accepted by American observers, for two years ago, when the writer contended that the first diarrheal manifestations were of central origin and compensatory in character, his views were acquiesced in by only a few students of pellagra.

Strambio distinguished two kinds of diarrhea, the one a dysentery characterized by frequent colicky and mucosanguinolent stools; the other more common, and characterized by watery discharges, frequent, and hard to control. According to him the dysenteric is more common in the earlier stage, but the serous or aqueous diarrhea belongs to the later and progressive stage, and is an important factor in producing the cachexia.

According to the experience and observation of the writer, this early diarrhea is often very watery, explosively ejected, and hard for the patient to control. This tendency to lose control of the anal sphincters soon after the advent of the first diarrhea has, so far as observed, been particularly noticed.

A recent case of this sort was a young widow, whose greatest complaint was her lack of control of her bowels, causing frequent soiling of her linen. At present she is better in many ways, but still reports difficulty in managing her sphincters.

The odor of these peliagrous stools is almost characteristic. To describe an odor is at the best unsatisfactory, but, like that exhaled from smallpox patients in the des-

quamative stage, or the peculiar smell of the vaginal discharges in uterine carcinoma, these feces have a distinctive odor. The feces are usually dark, often very watery, irritating to the parts over which they pass, and full of frothy bubbles of gas.

Several who have seen many cases of pellagra, and had occasion to often smell these foul stools, have expressed the belief that they could diagnose pellagra fairly well from the olfactory senses alone. In this somewhat bizarre statement the writer is tempted to concur.

The diarrhea, of central origin and compensatory at first, becomes eventually inflammatory in nature, partaking of all the symptoms of irritative diarrhea or ordinary dysentery. When this condition arrives, it is no longer compensatory or salutary in its effect, but rapidly saps the strength and reduces the weight. It is not uncommon to see a patient lose five to ten pounds in a week from such a cause. The diarrhea may even become choleraic, draining the body of its fluid in short order.

Should the disease progress favorably, and the patient seem convalescent, the whole digestive system remains below par for long after. The appetite is finical, the stomach easily upset, flatulence often in evidence; while the slightest indiscretion in either eating or otherwise is sure to result in a renewal of the diarrhea.

Can it be wondered that so many healed pellagrins become confirmed "nervous dyspeptics," afraid to eat a sufficiency for daily calories, and at all times sitophobic to a degree?

Before leaving the alimentary tract it might be well to mention that when patients complain of hemorrhoids, as

they frequently do, an investigation will reveal a proctitis, which will explain some of their "bearing-down" pains, and whose relief will greatly ameliorate the general condition.

It is the opinion of many that the digestive symptoms of pellagra in the United States run a more severe course than in Europe, especially in Italy. An idea prevailing in some quarters is that in those countries there has been acquired, either through heredity or some other manner, a gradual immunity, which has rendered the pellagrous toxin less able to make the rapid inroads observed in a newer soil for its invasion.

So much for the gastro-intestinal disorders of pellagra.

Nervous Phenomena.—Before entering into the psychic manifestations of this malady the more strictly nervous symptoms will be considered, though it will be impossible to keep the nervous and psychic separate at all times.

As has been admitted, many of the expressions are those of a trophoneurosis, and can be explained in no other way. The many pains, the burning surfaces, the quick and surprising changes in the aspect of pellagra from day to day, are necessarily the result of certain neuroses, some of them understood, some still obscure.

From the first fleeting pains, accompanied often by paresthesias and formication, to the flickering pangs of a disappearing neuritis, the last sign of the disease, nervous symptoms are in evidence practically the entire time.

One of the very first indications is a dysphagia, coming on intermittently and disappearing without reason. The patient naturally cannot understand such a phenomenon, comes to the physician for advice, and is surprised to find



This case shows a marked and extensive dermatitis over back and front of neck, face, forearms, hands, legs, and feet. Was transfused from sister, who had never had pellagra. Marked improvement for eight days. Died suddenly at night from perforation of intestinal ulcer. (Courtesy of Dr. H. P. Cole, Mobile, Ala.)

that the dysphagia has disappeared. It is then thought to be an hysterical manifestation, until other indications of pellagra are felt.

Early tremors are not rare, appearing somewhat like the tremors of disseminated sclerosis. These tremors are more marked in the hands than elsewhere, though the tongue is often affected. Frequently the patient is unable to stand with the eyes closed, swaying almost as much as in tabes.

An instance of this sort was under the care of the writer several months ago. The patient, a young lady of good circumstances and breeding, first noted the tremors on attempting to pass food on the table to other members of the family. These tremors in a short while began to affect her tongue, making her speech halting and uncertain. She found that she walked in the dark with difficulty and was timorous about walking alone. Her family physician, a gentleman of intelligence, thought it a beginning neurasthenia brought on by a period of religious excitement experienced at a series of services, which were led by an evangelist of the superstrenuous sort.

Soon after, she noted an intermittent diarrhea and indigestion, and in a few months the erythema confirmed the diagnosis already suspected. After a serious illness, in which nervous and psychic symptoms predominated, improvement set in, and she seems convalescent at this time.

Contractures are generally late symptoms and of grave prognostic import. The writer has not observed many, but others have met with contractures quite often in varying degrees of severity. These patients move with difficulty, are averse to any change of position, and sometimes,

in their efforts to find a comfortable pose, assume grotesque attitudes that would provoke laughter were the patient's condition not one of such misery.

A most remarkable case of this sort is narrated by Marie:

"In the case of one woman the skin was cadaverous and covered with telangiectases, the chestnut-brown hair scattered over with white and reddish spots, a rude beard, cranium ultrabrachycephalic, nose flat, teeth of the upper jaw worn away by constant friction, and, from this cause doubtless, a varicose nodule had formed on the tip of the tongue; emotional reaction was feeble, but not abolished; tactile and painful sensibility was much diminished; she was resistant; mentally she presented the picture of dementia precox of the depressed type and was mute; hid herself in fear in the most retired corners of the room or yard; if any one succeeded in making her talk, she did not seem to be deluded, but begged others about her to have pity on her misery, and was grateful for attentions received, of which she thought herself unworthy. All her inclinations and all her psychic activity expressed themselves in the most extreme muscular contractions. She sought the most favorable positions for contortions while hanging to slats and bars, to which she clung even with her teeth, her tongue, and toes. She gave as an explanation that she could not do otherwise. These symptoms continued up to her death, from tuberculosis, although in the last few days she uttered monosyllables—'good, bad, your kindness, so much misery,' etc. But up to the last day she continued to conceal herself as much as possible under the cover, and to cling with her feet to the bars of the bed."

We are informed by Italian writers that in some in-

stances laborers seem to feel a greater strength than usual when first attacked by pellagra. Such has not been observed in this country, but, on the contrary, weakness and uncertainty of the lower limbs are frequently noted among the first symptoms. There may be even pareses, though Tonnini, a contemporaneous Italian observer, claims that pellagrous paresis never attacks the muscles of respiration or those of the face alone.

Among other neuroses are muscular spasms, tetanic convulsions, epileptiform seizures, and sudden attacks of vertigo. Some of these muscular spasms produce very erratic movements, giving rise to some of the queer classifications bestowed upon the disease by uneducated people. These sufferers, during such attacks, fall backward or sidewise, or jerk in choreic fashion. These attacks are precipitated or made worse by external sensory impressions, such as loud talking, slamming of doors, etc.

Practically all pellagrins possess exaggerated reflexes, the normal or diminished reflexes being in a decided minority. Sometimes, though not often, there is a difference in the two sides, or ankle clonus is wanting.

The skin reflexes are generally either increased or decreased, seldom normal. When increased, the mechanical irritability of the muscles is in most cases also increased.

The electric reactions of the muscles and nerves have been studied by Roncoroni in the hospital of Turin. These experiments were made on four pellagrins, three of whom were in good physical condition. They did not display the reaction of degeneration and did not show any deviation, either quantitative or qualitative, from the normal.

In one case excitability was notably less than in the others, which was probably due to profound denutrition. This is not without interest for differential diagnosis from polyneuritis, progressive muscular atrophy, lateral amyotrophic sclerosis, transverse myelitis, and other diseases. He also found a greater faradic excitability of the flexors. According to him, diminution of the faradic excitability, even in the cases of spastic rigidity, is found in the third period of pellagra; under certain circumstances this reaction might serve as a differential diagnostic sign from spastic spinal paralysis.

In the majority of pellagrins, however, unless there are marked nervous symptoms, the ordinary gait is not materially changed.

Warnock says, "There is no special gait in early cases, but when the disease has become advanced the patient walks with the legs well apart, the shoulders raised and bent forward, and when he has reached the penultimate stage he cannot take more than a few short feeble steps without falling down, while in the last stage of all the patients are unable [to stand up or even raise themselves up in bed, and this paresis is sometimes accompanied by tremors of the limbs."

In the last stages, of course, the reflexes are all abolished.

The sensibility to touch and pain is in most cases of pellagra diminished, with the frequent exception of the area over the epigastrium and abdomen. "Out of 30 severe cases, Tonnini found five times a profound analgesia extending from the feet even to the face, but greater in the lower extremities; he found more or less analgesia fourteen

times and hyperalgesia four times. In 40 pellagrins less severely affected he found two-thirds analgesic and only two hyperalgesic."

" Hyperalgesia in pellagra is more common in florid types, and is accompanied by a decided elevation of temperature. The cases are numerous in which if they are touched, principally on the stomach or on the thorax, they begin to cry out, and at the least noise they start; others have painful paresthesias, as if water were thrown on their heads, or as if they were pricked on the legs by thousands of pins; they complain also of burning in the eyes, in the nose, and in the face. Insensibility to pain is often shown by their voluntary exposure to cold, as well as to burning or scorching, to which they repeatedly expose themselves. Tonnini found the sensibility to heat better preserved in the face than in the extremities, but sometimes cryesthesia is found."

These abnormal sensations of the skin and other parts of the anatomy, these aching pains and burning sensations, have been the bane of many of the pellagrins under the observation of the writer. In a number of instances, after seeing the patients safely through the gastro-intestinal disturbance, the eruption and the weakness, the manifestations of neuritis were so severe and obstinate that they have broken away, going from one medical advisor to another in frantic efforts to obtain relief. These are the invalids who readily become a prey to charlatans and quacks and all that ilk, who, by specious and misleading representations, extort "blood money" from these poor desperate sufferers.

The daily papers have recently carried advertisements of a vaunted "pellagra cure," where a tiny bottle was sold for

an unreasonable price, and where a guarantee to cure was included. To bolster up these ridiculous claims were printed letters from supposed pellagrins, claiming to be cured in from ten to *fifteen days*—God save the mark!

Cephalalgia of the severest sort is not uncommon. With the headache is ringing in the ears and dizziness. Dr. L. C. Allen mentions a patient of his, a fine old gentleman, who would often say, "I'm drunk, doctor, I'm drunk; I have not drank anything, but I'm drunk." He would often fall down and bruise his head. He died soon after.

With the exception of an occasional explosion of erotic passion during the incipiency, the sexual desire is either diminished or abolished in pellagra. This the writer has noted quite a number of times, and it does not seem to be mentioned specially in contemporary literature. In one instance, a middle-aged man consulted a specialist in Atlanta for impotence, not considering the concurrent symptoms of indigestion and diarrhea of importance. This physician became suspicious, and, on having the case thoroughly investigated, was able to inform the patient that the trouble was incipient pellagra.

The olfactories are not obtunded in this disease, but, as in some gastric disorders, often seem to be more acute. A young woman at the Tabernacle Infirmary in Atlanta informed the writer that she could detect and differentiate odors since her illness that would have been beyond her power during health. These patients, with squeamish stomachs at best, cannot eat or drink when their olfactories are offended, and this heightened sense is quite a problem to manage at times. The sense of smell is, in serious cases, about the last one to be lost.

The sense of taste must be judged by different standards. It is certain that bitter or very sweet articles can be distinguished, but all discriminating taste is soon lost in the presence of the sore tongue and mouth.

Another anomaly of sensation, and one of the most annoying, is the pruritus in the groins, or in the back and arms. Sometimes, in females, where the vulvovaginal margin is inflamed, this itching is so exasperating as to almost drive them to suicide. In a middle-aged lady, seen in the northern part of this state some time ago, this vulval and vaginal pruritus caused her more suffering than all her other symptoms.

The line of demarcation between the nervous and psychic manifestations is dimly drawn, and one merges into the other at nearly every point. The psychology of pellagra has not been studied long enough in the United States for much authoritative literature to have been accumulated. We are, to a large extent, dependent upon our studious friends in Italy and France for data in these protean manifestations of pellagra.

Some time ago the writer attempted to make some groupings of the psychic symptoms, but with nearly every new case a new viewpoint was brought to view, leaving the question more mixed and murky than before. With many misgivings, therefore, the difficult task will be undertaken.

Many pellagrins are quite sane, and always remain so, but there are few but who will admit a sense of mental depression, a feeling of misgiving, a vague unrest, or premonitions of impending disaster at some period of their illness.

The facial expression of pellagra, after two or three recurrences, is indicative of trouble and care. The deepened furrows attest the prolonged worry, and the oblique puckering of the eyebrows increases the grief-worn expression. The *facies* in pellagra is worth attention.

Insomnia comes on early and persists until convalescence is well under way. Very few pellagrins are good sleepers while the disease is making progress.

Among the first psychic symptoms are temperamental differences, perhaps not realized by the patient. Unreasoning discontent at petty discomforts and unreasoning anger at slight annoyances are not uncommon.

Two years ago a gentleman from a neighboring state was under treatment, whose first symptoms were a dislike for his two little children, of whom he had previously been very fond. Their childish prattle exasperated him, and he admitted that he could not understand why. These peculiar feelings of antipathy for his children lasted six or more months before any other manifestations of a pellagrous nature became patent. He then began to suffer from indigestion, loss of weight, and diarrhea, and in a short while the tell-tale erythema of the hands furnished the last necessary link in the diagnosis.

Next the patient finds that thinking or calculating is an effort; he becomes irritable or excitable when in the company of others, or morose and despondent when alone.

In the intermittent type there is seldom any decided symptoms before the second recrudescence, but after that a settled gloom begins to fall over his spirits. He is sad, uninterested in what is going on about him, but contentious for his own rights. His sleeplessness is troublesome,

his surroundings are distasteful, and he evinces a desire to wander away. Sometimes a sense of having committed a dreadful crime comes over the mentality, and fears of detection and punishment are added to the burden, heavy enough before. Obsessions of having injured loved ones, of having been guilty of some loathsome transgressions against the laws of God or man, fills the sick soul with grievous remorse.

Sometimes, with the burning and itching sensations, comes the delusions of being burnt. There are also frequent delusions of persecution. With negroes the thought of being bewitched is uppermost in their minds, and they seek strange charms and curious objects, which they think have the power to drive away the evil and torturing spirits. These poor creatures are easily frightened, easily panic-stricken. They seek escape in flight, and hallucinations of poison often make them refuse food and drink to the point of inanition.

As in some other delusional insanities, they are prone to feel the greatest antipathy for and fear of their dearest relatives and friends, attributing sinister motives to all attempted acts of kindness.

As the descent into Avernus is swift, so the mental decline is rapidly progressive, deepening from discontent to sadness, sadness to melancholy, melancholy to confirmed melancholia, and on down the psychic decline to dementia.

The writer is informed by one alienist that about half the pellagrins who applied to him were already melancholic, though not at the time insane.

Dr. Holland, in describing these symptoms, said, "The pellagrosi complain of a sense of heat in the head and

spinal cord, of tingling and darting pains in the course of the nervous system, of heat in the limbs, palms of the hands, and particularly in the soles of the feet; of great weakness of the limbs, with trembling when attempting to stand, and sometimes of contractions of the lower limbs. Their looks become somber and melancholy. Ennui, depression of spirits, and mental imbecility increase with the progress of the malady." He also states the pellagrosi afford a melancholy spectacle of physical and moral suffering at this period. They seem under the influence of an invincible despondency, they seek to be alone, scarcely answering questions to them, and often shed tears without obvious cause. Their faculties and senses are impaired, and the disease, when it does not carry them off from exhaustion of the vital powers, generally leaves them insensible idiots, or produces attacks of mania, soon passing into utter imbecility or idiocy.

The following case, as reported by Sandwith, shows several sides of pellagra manifested in one patient, but particularly the psychic aspect, "M. H., an Egyptian peanut woman, aged thirty, was admitted to Kasr Ainy on April 17, 1897. She had a well-marked pellagrous eruption, was thin and weak, and abnormally hungry. She passed her excreta in bed or anywhere in the ward, and had to be prevented from eating dirt. She was melancholic, unwilling to talk, and when spoken to she repeated the question and seemed unable to reply. At night she would get out of her bed and walk about the passages. She had favus all over her scalp, and ankylostomiasis, which required four doses of thymol. We afterward found from her relations that one morning she had gone down



Well-marked manifestations of pellagra. (Courtesy of Dr. Beverly
Tucker, Richmond, Va.)

to the river to bathe, and had then wandered some miles along the river bank until she reached Cairo. On October 9th she was discharged from the hospital, having increased in weight thirty-two pounds; she now smiles, talks, helps the other patients in the ward, understands all that is said to her, and seems quite sensible; she has no eruption, and her tongue is quite normal. Her knee-jerks are still too brisk, and she still weeps rather easily if she has any disagreements with the other patients."

The writer, not being an expert alienist, feels disposed to defer to those who have more thoroughly tilled the psychic field, and have garnered a more seasoned burden of scientific ideas. As such, Dr. J. W. Babcock stands in the forefront, and the remaining discussion concerning the psychology of pellagra is extracted from his recent paper, "The Psychology of Pellagra," being made up of his own views and the views of others, as collated by him. Hack Tuke studied pellagra in Italian asylums in 1865. He says, "The patients were in advanced stages of the disease, and were all more or less emaciated, sallow, anemic, and presenting a miserable dry, wrinkled skin. They were obtuse and inert, their mental state being that of dementia, quiet, chronic mania; or, in some instances, chronic melancholia. None of them was in an acute maniacal condition."

The views of Salerio, director of the asylum of San Servolo, Venice, upon the mental condition of his patients, may thus be summarized, "They are generally frightened; think they are pursued or possessed of a devil, suspicious, refuse food and medicine, and have exalted religious notions. Suicidal tendencies may be present. Homesickness is

common and severe. Finally, they are liable to lapse into dementia, paralysis, or tubercular diseases."

Bucknill and Tuke quote also from an early work of Lombroso, who thought that one characteristic of pellagrins, sane or insane, was the greater moral impressionability. A slight insult, the threatening of some trivial danger, completely carries them away. If pellagrous insanity assumes a type, it approaches rather that of chronic mania and dementia than that of monomania. This Lombroso ingeniously terms "psychical catalepsy." But, as a rule, their sanity is of a misty, ill-defined, contradictory character, like that produced by old age or by anemia, and differing on this point from general paralysis.

Morselli gives four forms of pellagrous insanity, viz., supra-acute pellagra (typhoid pellagra), pellagrous melancholia, pellagrous dementia, and pellagrous pseudogeneral paralysis.

Babes and Sion say, in part, "Usually after several years of somatic pellagra, psychic symptoms come into prominence. At first the patients experience mental weakness. The peculiar pellagrous lunacy is preceded by spasmodic, then tonic, cramps and general bodily weakness, and advanced to true pellagrous paralysis. The cramps of feet, hands, and calf muscles are sometimes so violent that they may result in epilepsy, contractions, and swooning. So-called pellagrous epilepsy occurs as the result of spinal pain, the patient being drawn backward. An important condition, called pellagrous tetanus, has been described by Strambio, opisthotonus being a common characteristic symptom. Sometimes the patients are drawn forward and fall to the ground. Chorei-

form movements, especially of the head, are observed, generally from the incipiency of the disease; depression and weakness of the memory are noted. Roussel asserts that in this stage deliria do not appear, but that they come on in the spring of the second or third year. The sadness may advance to mutism and refusal of food; these conditions often being interrupted by lachrymose or maniacal or suicidal episodes. An acute attack leaves the patient exhausted, depressed, and hypochondriac. Such attacks recur annually at about the same time, the intellect weakens, and gradually dementia develops.

"Pellagrous melancholia shows various stages: at first, there are psychic impediments, followed by apathy or stupor. Delusions of sin, of persecution, etc., appear. Mania is rare, but catalepsy sometimes occurs.

"When paralysis supervenes, euphoria appears, presenting a disease-complex like general paralysis, but even in advanced stages of the disease remissions may occur."

G. Antonini writes, "Already, in the first stages of pellagra, there appears a decided modification in the mental faculties; there is a great impressionability, a greater psychic excitability; a slight disappointment depresses greatly the tone of feelings or produces excessive reactions (from the want of initial inhibitory powers). In the progress of the disease we can have true amentia, states of mental confusion common to all psychoses arising from exhaustion. This state can show suddenly an aggravation of symptoms and lead to death with a syndrome of acute delirium (typhoid pellagra), and yet it can also present in certain cases a true progressive paralysis of pellagra.

"But a frequent symptom is the obstinate refusal to take food, such as aggravates painfully the already sad picture of the pellagrin."

Griesinger notes that pellagrous insanity, according to Clerici (1855), consists chiefly in a vague, incoherent delirium, accompanied by stupor, loss of memory, and by loquacity without special disorder of intelligence or violent excitement; the melancholic state, which predominates for a long time, always passes gradually into a state of torpor of all the mental powers, with muscular weakness, which greatly resembles general paralysis.

Mongeri concludes that the pellagrous psychoses begin, ordinarily, with a period of mental depression accompanied by hypochondriac ideas. Following great mental prostration the ideas become confused. Later melancholia appears, accompanied by hallucinations of hearing, with illusions of general sensibility. Following this condition are delusions of persecution with a tendency to drowning (the hydromania of Strambio). Again, developing persecutory paranoia, pellagrins commit crimes of every sort (homicide, infanticide, incendiaryism, etc.). Dementia is the common termination.

According to Bianchi, one of the leading modern Italian writers, "The nervous phenomena dominate the scene in pellagra. We may classify the different varieties in two groups, the chronic and the acute. The first is characterized by general depression, melancholia, confusion, slow dementia, paresthesias, and ataxic gait. Contractions and subsulti are absent, although in most instances the reflexes are exaggerated. In the acute form we have elevation of temperature (39° to 41° C.), intense neuro-

muscular excitement, subsulti, contractures, muscular rigidity, exaggerated reflexes, and confusion with phases of exaltation. There are numerous intermediate forms in which we observe a great variety of psychic phenomena, and also alternation of excitement and depression. Phases of remission and of apparent recovery are observed, especially at certain seasons."

Regis announces that, "It is recognized that the most common form of psychosis in pellagra is mental confusion, with melancholy or dreamy delirium. This occurs more or less marked in most of the cases. It is manifested by an inertia, a passivity, an indifference, a considerable torpor; by insomnia, hallucinations often terrifying, both of sight and hearing; by delirious conceptions, with fixed ideas of hopelessness, of damnation, of fear, persecution, poisoning, anxiety, of possession of devils and witches, of refusal of food, and so marked a tendency to suicide and to suicide by drowning that Strambio gave it the name hydromania. This melancholy depression, which can reach, in certain cases, even to stupor, is always based upon a foundation of obtusion, of intellectual hebetude, and of considerable general debility, which becomes permanent and terminates by degrees in dementia, in proportion as the pellagrous cachexia makes new progress. It is accompanied sometimes by a polyneuritis. The mental confusion of pellagrins can, in place of changing directly into dementia, turn to a chronic mental confusion.

"One may also observe in pellagra, as in every chronic grave intoxication, a morbid state resembling general paralysis (pellagrous pseudogeneral paralysis). This occurs especially in the cases where, instead of habitual

melancholy ideas, the patients present ideas of satisfaction and of wealth."

Procopiu discusses the subject at length, saying in part, "We have seen that the character and intelligence of pellagrins change. They become sad, apathetic, silent; in the more advanced stage they are melancholy, and fall sometimes into an absolute mutism or respond with difficulty, and have the air of not understanding what is said to them.

" Sometimes this melancholy is accompanied with stupor, and leads the poor pellagrins into dementia.

" It is not rare in this condition that an attack of acute mania breaks out. At another time the attack of mania breaks forth suddenly without apparent cause, or under the influence of a sunstroke, a quarrel, a disappointment, etc.

" Sometimes it is in the spring that the excitement, as the other symptoms of pellagra, makes its appearance, but generally it is later than the others, and bursts forth at the end of the season or even during the summer.

" Pellagrous insanity has been divided into acute and chronic forms. The acute form is more frequent when the pellagra is associated with alcoholism; then this form presents the characters of delirium tremens. The acute form often manifests itself in the course of the chronic form, but it can also begin in the state of apparent health.

" The acute insanity, in particular, which bursts out suddenly while the patient is in a state of mental health, is easy enough to cure. But when the disease is advanced, and the lesions of the nerve-centers are profound, cure is difficult, sometimes impossible, especially in the case of dementia. When even a sensible amelioration is obtained,

the intellectual condition of the patients remains always in a marked degree of inferiority."

From the more recent treatise of Tanzi, we learn that "pellagra is almost always accompanied by psychic disturbances, which often have the character of true mental diseases.

"A pellagrous melancholia and a pellagrous mania have been described. The characteristic psychosis of pellagra is, however, amentia, which manifests itself acutely in loss of sense of place, loss of memory, confusion, hallucinations, and paresthesias, from which there arise morbid impulses and delusions. Pellagrous amentia often assumes a depressive form which simulates melancholia, and in some cases, either from time to time or throughout the whole course of the psychosis, it is accompanied by exaltation, which gives it some resemblance to mania.

"The first attack of amentia occurs after pellagra has existed for some years and has already given rise to erythema and diarrhea, and has remitted from time to time. In other words, the pellagrous lunatic is, as a rule, a chronic sufferer from pellagra. But while the pellagra, although chronic, continues to run an intermittent course, the mental disturbances associated with it have the characteristics of an acute insanity, which corresponds exactly to amentia, *i. e.*, to the most typic of the acute insanities, both as regards the symptoms and course.

"The insanity of pellagra is thus something different from common melancholia or from ordinary mania. It is also something more than simple amentia. We may regard it as the combination of two distinct clinical pictures; namely, that of amentia in the first attacks, and that of

dementia in the later and progressive phase, marked by chronic and incurable cachexia. It is an intermittent and progressive amentia, which, if not cured, or if not early fatal, terminates in dementia."

Babcock here inquires what is the relationship of pellagra to progressive paralysis?

"Baillarger asserts that pellagra may be followed not only by mania and melancholia, but also by progressive paralysis. Verga opposes the last opinion, while Regis and Piannetta affirm it."

Gregor, in 1907, recognizing that exhaustive clinical observations on the so-called mental disturbances of pellagra were wanting, made careful analysis of the psychic condition observed in 72 cases who had been admitted to the Bukowina State Asylum from March, 1904, to September, 1905. In 1902, he says, Finzi published his "Psicose Pellagrose," coming to the conclusion that this mental disturbance is essentially an insanity, and that the psychosis of pellagra is amentia. This view, which agrees with that of Tanzi, was combated by Vedrani, who maintains that the psychosis of pellagra takes usually its course without serious disturbances of orientation and reason. On the other hand, Warnock claims that symptoms of melancholia are the usual accompaniments of the mental disturbances in pellagra, and thus approaches the views of the older writers, who assumed especially close relations between pellagra and melancholia. Thus Aubert tried to prove, in 1858, that an attack of pellagra might convert a heterogeneous disease into melancholia. This view was vigorously maintained by Aubert against Baillarger and others, who held that the psychoses of pellagra



Well-marked vesication of temporal and mastoid regions, known as the
“butterfly.” (Case of Dr. G. A. Zeller.)

are polymorphic, including meningitis, mania, melancholia, etc., and even general paralysis. This view is still maintained, notably by Zletarovic, who has observed the development on the basis of nutritive disturbance caused by pellagra of melancholia and mental weakness to complete stupor and dementia, but he never observed mania. Even Lombroso and Tuczek, says Gregor, give only pictures of psychic conditions. Gregor also considers the studies of pellagrous insanity by Finzi and Vedrani as inadequate, but, granting the absence of a characteristic symptom-complex, he says that we must still search for characteristic peculiarities, since psychoses, which are in themselves not specific, may assume certain symptoms which are to be considered with regard to their etiology.

Gregor also included in his study whether the relationship between pellagra and the psychoses was accidental or casual. It will thus appear that he attempts to reach a much broader and deeper conception of the neuroses and psychoses of pellagra. He divided his 72 cases into seven groups: (1) Neurasthenia, (2) acute stuporous dementia, (3) amentia (acute confusional insanity), (4) delirium acutum, (5) katatonias, (6) anxiety psychoses, and (7) maniac-depressive insanity.

In the following summary Dr. Babcock gives Gregor's analyses:

"*Neurasthenia*.—The symptoms of Gregor's first group in their details are not specific of pellagra, but offer in their totality a characteristic disease-picture.

" The symptoms are subjective, and include headache, pain in the gastric region, vertigo, paresthesias, lassitude, depression, a sense of unrest and anxiety, which may be

raised to a phobia, as well as ill-defined apprehensions. There is also a sense of bodily and mental incapacity and of illness. Their conduct is normal, and the intellect may be unimpaired, but they are incapable of mental and physical exertion. The process of association is distinctly disturbed, the simplest question often being answered only after prolonged hesitation. With depression of spirits, hypochondriac notions may develop from a consciousness of being pellagrous, or experience in former illnesses. In some cases there is a slight motor unrest and a desire to move about, but, as a rule, patients of this group labor under motor impediment, and sink finally into a condition of apathy and resigned inactivity. Gregor admits that these symptoms are not specific of pellagra, but he suggests that, if these symptoms have lasted for several years, the suspicion of pellagra as a causative factor should be aroused in the physician's mind, even without the presence of the somatic stigmata of the disease. He also observed that the first attack of pellagra is more likely to be accompanied by neurasthenia, and that this condition commonly preceded the development of the pellagrous psychoses.

"Acute (Stuporous) Dementia."—The milder cases of this group differ from the preceding group only in degree. The symptoms, merely suggested in the former group, exist here in full force. The cases of this group are characterized by a distinctly marked stupor, tending to remissions, by deep mental depression, a vivid sense of insufficiency, and peculiar subjective troubles. The dependence upon pellagra intoxication can be established by the close connection of the psychic disease-picture with the somatic symptoms of pellagra. The mental symptoms

improve with the bodily. The external appearances, the depressed mental condition, the tendency to suicide, etc., explain the fact that such cases are frequently considered melancholia. Finzi contradicts this view, and places these cases under amentia. Some of Tanzi's and Vedrani's cases come under this group.

"The patients give the impression of being sick, as they lie still and apathetic in bed for weeks, and answer repeated questions only after a painful effort, or not at all. Requests of the simplest nature are carried out only with hesitation and effort, and often the action once begun is interrupted in its first phase, or the request is forgotten. Mostly we are assured that the patients are well oriented, and often we see, after the hesitation ceases, that the psychic activity is revived for a short while, but, sometimes in the height of the disease orientation may be disturbed. Illusions appear, the patients show a sense of insufficiency, and sometimes also a hypochondriac sense of sickness and a consciousness of their psychic impediments.

"In many cases, in which the stupor developed gradually, a disturbance of psychomotor activity was observed without vivid mental disturbances. On the other hand, some cases, recognizing their incapacity for practical life, voluntarily committed themselves to the asylum. Most cases showed a gradual development of an affectless stupor, with a final return to their former mental condition. Rarely, psychic impediments develop in a relatively short time. The sense of insufficiency may assume a distinctly melancholy coloring, with suicidal tendencies. Again, severe cases may assume temporarily katatonic symptoms of posture and motion stereotypies.

"With this group memory disturbances were especially well marked, as Tanzi has emphasized, but weakness of memory is not a characteristic of acute pellagrous dementia. Upon convalescence memory returns easily, so that the apparent memory disturbance is due rather to the general difficulty of performing psychic processes than a weakness.

"With the relief of the somatic symptoms of acute pellagra the mental symptoms also improve. Besides, the connections between pellagra and nervous disturbances is evident, and different mental symptoms may complicate the picture. It would appear that melancholia is the typic mental disturbance of pellagra. Tanzi believes that we should call such cases amentia, and consider them light forms of this psychosis. It is in this group that Tanzi would place the typic cases of pellagrous insanity. Stupor seems to promise a long duration and an unfavorable prognosis. Favorable cases lasted from one to six months.

"Amentia (Acute Confusional Insanity).—These cases were long continued, with a tendency to remissions and intermissions. After a prolonged period, which shows essentially the symptoms of the first group, appear usually terrifying hallucinations, accompanied by violent motor excitement. The delirium was frequently followed by stupor or existing stupor was interrupted by delirium. The patients see the house or village burning, enemies coming, wild animals attacking them, the devil appears, or machines cut off their heads. More rarely, they have quite dreamy states, the heavens open and the Lord appears, bishops, priests, figures pass by. In imagination, they return to the scenes of their daily life. Again, they

run away to escape the flames or to defend themselves against persecution. Here we have phenomena of motion in connection with hallucinations. If secluded, they move about, are noisy, and knock upon the door. The duration of this excitement varies from a few hours to several days. These episodes are followed more or less by long intervals, in which the patients are quiet in mind and body. They may be stuporous, but usually show only slight disturbance of orientation. Later, they pass into a delirium like that of meningitis or typhoid. If diarrhea be present, the complex of typhoid pellagra is recognized. This may develop in a chronic case or be an acute process, while in rare cases the bodily and mental symptoms may improve. Death usually follows this typhoid condition. Hallucinations seem to offer for the first attack a decidedly favorable prognosis.

"Dementia does not always ensue upon a severe initial attack, but develops in chronic cases of either bodily or psychic pellagra. The development of katatonic symptoms, which may appear especially in youthful cases, renders the diagnosis difficult.

"*Acute Delirium.*—The cases of this group are distinguished from those of the third group by the intensity of the disease symptoms, hallucinations, motor excitation, and shorter courses in death. For this reason the conception as acute delirium seems justified.

"The symptoms of this condition may occur without the bodily signs of pellagra, but they usually occur synchronously. Absence of a rise of temperature has been noted by both Italian and German observers.

"Groups 2, 3, and 4 show a great similarity with the

mental symptoms of acute infectious diseases. They might therefore, be classified under the infective exhaustive psychoses.

“*Katatonia*.—The katatonic condition occurs with the acute somatic pellagra. Here, considering the concurrence of acute somatic and psychic pellagra, we must assume a pellagrous intoxication as to the causative factor, as in pellagrous neurasthenia. Many patients show consciousness of their disease. Hallucinations may precede this condition. Excitement, stereotypy, wild jactitation, and verbigeration are common. The katatonic cases pass rapidly into dementia.

“Of the cases of the fifth group, the majority belong to the katatonia subdivision from the symptoms, courses, and termination. In three cases (females) excitation occurred, ending with stereotypy, jactitation, and verbigeration. The patients did not show marked affects. In one case hallucinations preceded the condition. In all three cases the transition into dementia was rapid, in which posture and motion stereotypies, impulsive actions, and talkativeness were observed. In one case these symptoms were followed by a permanent negative phase. In another case, besides many posture and motion stereotypies, interchange of negativism was observed. In one case the katatonic symptoms were marked from the beginning. A male case showed, on admission to the hospital, katatonic excitations, and after a few days a remission followed by another katatonic phase. Six of these cases ended in dementia more or less rapidly, although remissions occurred.

“*Anxiety Psychoses*.—The violent, fluctuating anxiety

effect, the motor unrest, the anxiety ideas, and the ‘phonemes’ completing them, determines from the first the diagnosis of an anxiety psychosis. It is true, this disease-picture is complicated by extraneous features. The patients show a marked sense of insufficiency, appear slightly stuporous in the intervals between the attacks, and resemble cases of groups 2 and 3. Later the anxiety attacks have disappeared, the mental weakness increases; the second phase gradually lessens as it does in patients of the mentioned group. In the second case the psychomotor weakness changed by turns, with violent anxiety effects and vivid motor unrest. Temporary ideas of persecution and of sin, and, later, of stupor were also observed. The third case was typic depressive melancholia.

“*Maniac-depressive Insanity*.—Of the two cases, one showed the condition of mania arising from subjective pellagrous troubles. In the other, mania was followed by distinct stupor.”

The dementia following pellagra shows different forms. One form develops an almost complete disappearance of mental activity, which justifies the name “paralytic.” But a milder degree of dementia characterizes the larger number of cases. They are oriented, usually well behaved, but dull, and showed a lack of self-restraint, with a tendency to break out into violent passions and impulsive actions.

A simultaneously existing alcoholism has a modifying influence upon the disease-picture. Furthermore, in many individuals, the pellagrous mental disturbance does not appear until old age, and it brings about a precocious senile dementia.

There is a distinct pellagrous dementia, like paresis, marked with somatic changes. An affirmative answer is given to the question, Are there disease-pictures of dementia whose anatomic basis is an injury to the brain by the toxins of pellagra?

As to the broad classifications of the different psychoses of pellagra, probably our most practicable one has been given us by Dr. J. W. Mobley, of the Georgia State Sanitarium. He says that his cases fall principally under the intoxication or infective-exhaustive group, and he has subdivided them under four headings:

- (1) Acute intoxication psychosis, with psychomotor suspension.
- (2) Infective-exhaustive psychosis, with psychomotor retardation or excitation.
- (3) Symptomatic melancholia, with psychomotor retardation.
- (4) Maniac-depressive, with psychomotor retardation or excitation.

That the various psychoses are of the most complex nature can be inferred from the learned opinions so well brought to our notice by Dr. Babcock. That the manifestations of the subtle poison on the psychic centers may be influenced largely by temperament, environment, previous health or habits, or individual idiosyncrasies is admitted. Finally, when we thoroughly understand what the toxin of pellagra really is, then may we better read these many shades of disturbed mentality, ephemeral or lasting as they may appear, and with that knowledge better be able to minister successfully to these sick souls.

So much for the psychology of pellagra.

Ocular Symptoms.—While the ocular symptoms in pellagra are not distinctive, there are some abnormalities that are of interest to consider.

Dr. E. M. Whaley, of Columbia, studied this aspect, and has drawn some interesting conclusions.

He found that pellagrins did not carry their upper lids as high as they should, giving them the appearance of lassitude. This has often been noted by the writer, and mentioned some months ago. Dilated pupils are not the rule, though hypersensitiveness to light with contracted pupils was frequently noticed. Shallow anterior chambers were found by Dr. Whaley in one-third of the cases.

A peculiar lack-luster expression of the eyes has been observed in a majority of the cases, and, in the negroes the brownish pigmentation is deepened until it presents almost a jaundiced look. Pupillary inequality is not uncommon. It may be said, however, that eye symptoms with pellagra do not seem to be as frequent in pellagrins in the United States as in Europe, according to the reports in hand.

The **thermal phenomena** in pellagra have been the subject of much study. That the conclusions reached by observers of cases in private practice and physicians in hospitals or asylums should show a variance is not surprising. One writer, in reporting on 100 pellagrins whose temperature had been recorded for a month, found more or less fever in 80 per cent. This occurred in an asylum, and it is reasonable to suppose that both degenerative and inflammatory changes would be found in greater proportion than in a given number outside of such an institution.

It has been the experience of the writer in a large number of pellagrins that, in uncomplicated, ambulatory

cases, the temperature was practically always normal or subnormal—often the latter. Many of these pellagrins easily “caught cold,” which would give rise to a temporary rise of temperature, but, apart from the typhoid condition of pellagra, which will be considered later, the pellagrous process is essentially afebrile.

Should this disease progress to the “third stage,” as some classify it, where there is more or less autotoxemia exerting its irritating effect on nearly every organ in the body, there is, of course, a natural tendency to febrile exacerbations, along with the other abnormal manifestations of the diseased body.

There are occasional fulminant cases, where a high temperature prevails from the onset of the malady, and where a beginning improvement, if the patient is so fortunate as to experience it, is ushered in by a decline in the febrile symptoms.

Many of the ambulatory cases habitually run a subnormal temperature in the forenoon, barely getting to normal later in the day.

The writer has records of over 25 of such cases, where they were regularly observed in the forenoons, and in but few instances was the temperature ever found above 97.3° F.

Sandwith positively and laconically sums up this question by saying, “The temperature of an uncomplicated case of pellagra is always normal or subnormal.”

The last phase of the different clinical forms in which this protean disease is manifested, and the consideration of which will close this chapter, is aptly termed *typhoid pellagra*.

The fact that pellagrins may and do have typhoid fever should be remembered. Watson mentions seeing two cases of typhoid in pellagrins in 1910, and the writer saw one typic case in which not a single classic symptom of typhoid fever was lacking.

According to Scheube, typhoid pellagra (*typhus pellagrosus*) consists of an aggravation of all the symptoms, especially the mental. His description is as follows, "The whole muscular system is in a condition either of rigidity or intense tonic contraction. The head is buried in the pillows and at times convulsively moved. On spontaneous movement of the limbs a perceptible trembling and indications of inco-ordination are made manifest, and tremors and fibrillary contractions are seen in the face from time to time. The speech is drawling, tremulous, and often exhibits a nasal twang. Frequently there are hyperesthesiae and heightened reflex excitability, the tendon reflexes in particular being always increased."

As to the increased tendon reflexes, this has not been observed by the writer, but rather the reverse.

The temperature is generally high, and may run rather a symmetric course, not unlike true enteric fever, but this typhoidal condition may supervene, progressing to a fatal issue without any rise of temperature.

Procopiu thinks this condition due to the Eberth bacillus in the intestines, in which event we have both pellagra and typhoid fever. His views are not accepted by many observers.

The typhoid condition of pellagra generally ushers in the terminal stage, and occurs after the patient has suffered perhaps several recurrences. There is noticed a more

rapid failure of strength, a more noticeable decline in the mental powers, and an increase of all the gastro-intestinal symptoms. The abdomen becomes distended, the diarrhea becomes more intractable, and the stools are often involuntary and passed without the knowledge of the patient. The stools also take on that dreadfully foul odor of which mention has been made. The watery feces are acrid and irritating, and the mucocutaneous areas in and around the anus or vulva become raw, perhaps bleeding, when cleansed.

The heart, kidneys, and lungs may become involved as in any other acute exhaustive condition, and a low delirium, with subsultus, opisthotonus, muscular rigidity, convulsions, and all that melancholy picture of a system succumbing to a long-continued toxemia.

This typhoid condition, which in itself has no relation to typhoid fever proper, is nearly always fatal, seldom lasting over two weeks.

COMPLICATIONS

In the clinical course of pellagra there are a number of complications liable to occur.

The mental complications have been sufficiently covered.

In Egypt Dr. Sandwith considers ankylostomiasis an almost invariable accompaniment, often joined with bilharziasis. The ankylostomiasis anemia predisposes to other complications, as wrist-drop, paraplegia, general tumors, epileptic seizures, all following degeneration of the spinal cord; also retention of the urine; herpes zoster and bronchitis are often noticed. Malaria, too, is a frequent complication.

In the United States, especially, both the *Uncinaria americana* and the *Amœba coli* are frequently found in pellagra. Among some investigators the ameba has so often been found in the stools of pellagrins that a common causative factor has been surmised. Pyorrhea alveolaris, with accompanying ameba in the pus-pockets about the teeth, is not uncommon. Occasionally a supposedly pellagrous sore mouth with free diarrhea will quickly disappear under appropriate amebacide treatment.

One of the most fatal complications is acute alcoholism. The pellagrous condition seems to be affected in a specially malign manner by alcohol, especially in the form of whisky, and it has been frequently noted that hard drinkers almost invariably run a speedy and fatal course.

About a year ago the writer treated an acute case of pellagra in the Tabernacle Infirmary in a robust man of forty-five. All the symptoms of a typic case were present—the sore mouth and tongue, the erythema on arms, feet, and face, the diarrhea, and the mental depression—not a symptom lacking. Under the influence of treatment he improved rapidly, seeming convalescent in about four weeks. He was known to be addicted to whisky, occasionally getting under its influence, and he was particularly cautioned as to the danger of indulging in this stimulant. In spite of his promises, however, soon after his return home he fell into an alcoholic debauch, in which he exposed himself to the rain and cold, and otherwise mistreated his body. The pellagrous symptoms immediately returned with increased virulence, terminating his life in less than two weeks.

Syphilis is an occasional complication, but, apart from its added burden, has no special bearing on pellagra.

In Lombardy, where there is much goiter and cretinism, we are informed that the physicians there regard one disease as the cause of the other. In the United States thyroid disease has been noted in connection with pellagra to some extent. Dr. D. P. Curry, Sanitary Inspector of the State Board of Health of Kentucky, has noted goiter in quite a large proportion of pellagrins coming under his care.

Dr. E. G. Jones, of Atlanta, who has perhaps observed more cases of goiter than any one in the South, gives as his opinion that concomitant pellagra and goiter are not more frequent than concomitant nephritis and goiter, syphilis and goiter, or tuberculosis and goiter. He believes, however, that pellagra may exert an influence in "lighting up" a latent goiter, or that hyperthyroidism may, in the same manner, bring out a latent pellagra.

One of the most difficult complications to manage is the condition of marasmus or wasting away, into which the pellagrin sometimes lapses. A liberal diet seems to aid not at all, and emaciation rapidly supervenes, bringing with it apathy, mutism, lessened tendon reflexes, and muscular rigidity.

The writer has at present under observation a case of this sort, and, while the patient is eating fairly well and being given the most nourishing food, the emaciation is progressing, and the prognosis is extremely doubtful.

Pregnant pellagrins seldom go to full term, generally aborting before the sixth month.

Among the gynecologic complications are amenorrhea in the nulliparas and menorrhagia in the multiparas. Among



Pellagra in the negro. (Case from State Hospital for Insane, Columbia, S. C.)

other ills in this category are vulvitis, vulvovaginitis, cervical erosions, endocervicitis, endometritis, and leukorrhea. Ovarian neuralgia, along with the other nerve pains, is present in nearly every female pellagrin. Where there have been previous gynecologic troubles, which have been seemingly allayed, an onset of pellagra sets up a renewal in many instances.

Appendicitis in the course of pellagra has occurred once in the service of the writer at the Tabernacle Infirmary Annex (for Pellagra). The patient, a young unmarried woman of twenty-five, while apparently progressing favorably with her pellagrous infection, was suddenly attacked with acute appendicitis. Palliative measures having failed to give relief, she was operated on by Dr. J. L. Campbell. The appendix, which was removed, was hard, indurated, and dry. After the operation the recovery was uneventful, the wound healing by primary adhesion. The operation did not seem to unfavorably affect the pellagrous process, while the removal of the diseased appendix exerted a decidedly beneficial effect on the gastro-intestinal symptoms. At present this patient seems to be quite well.

This practically covers the more frequent complications, though in the presence of pellagra, as in any other disease of an exhausting character, intercurrent affections are liable to crop out at any time. Therefore, while watching for the direct and indirect manifestations of pellagra proper, it is well to be on the *qui vive* at all times, lest some unexpected complication, in the already strenuous battle, diminish the outlook for recovery.

CHAPTER V

CLINICAL REPORTS AND DESCRIPTIONS OF CASES OF PELLAGRA FROM DIFFERENT SOURCES

THE previous chapter has purported to cover the symptomatology and clinical history of this disease as it has appeared to various observers in different parts of the globe. In a malady of such varying shades it is but natural that it should leave different impressions upon the medical attendants in closest contact with the sufferers.

It is thought wise, therefore, to incorporate in this chapter a number of clinical histories from widely scattered localities, in the hope that the reader may obtain a broader conception of this disease entity, whose presence has become a problem to both the student of medicine and the publicist.

The first report is the graphic description of a case in Virginia, as reported by Dr. J. H. Hewett, of Lynnhaven:

Patient.—H. A. S., London Bridge, Va., aged fifty-six, white, widower, occupation milling and farming, was born in Charlotte County, Va., reared in Pennsylvania County, and remained there the greater part of the time till February, 1909, when he moved to Princess Anne County, Va. He had spent a year each in Roanoke and Lynchburg, Va., where financial reverses made him poor. He also spent three years in Nebraska, and then returned to Virginia.

Family History.—The patient's father was killed in an accident at the age of forty-eight; his mother died of old age at eighty-four. Two brothers are living and well. Two brothers are dead—one of "Bright's disease," the other of "brain fever." Five sisters are living and well. There is no history of cancer, tuberculosis, rheumatism, or insanity in any member of the family. The patient's father and two of his brothers always suffered from diarrhea whenever they ate bread from corn-meal.

Personal History.—During childhood the patient had diphtheria, measles, mumps, and pertussis. He had typhoid at eighteen, malaria and gonorrhea at twenty-six, grip at thirty-five. Since thirty-five he has always been well till the present illness. He has noticed that bread made from corn-meal always disagreed with him, even in childhood, producing diarrhea and intense intestinal pain. His father and two of his brothers, as above stated, were also similarly affected by corn-meal bread, but he has no knowledge that any of them ever suffered with roughness and desquamating of the skin at any time. His average weight is 145 pounds. He uses tobacco and alcohol moderately. He is the father of seven children, all of whom are dead. The second child died at the age of thirteen. His wife died sixteen years ago. They lived together eighteen years. He denies lues.

Present Illness.—The patient is now a very poor man, and for the last three years has been living in cheap boarding-houses or keeping bachelor's quarters, in which he did his own cooking. During the latter part of last fall, owing to the scarcity of work and the high price of flour, he was compelled to eat more and more corn-meal. About the

middle of last December his present diarrhea began, very mild at first, but slowly and steadily increasing in intensity until about six weeks ago, when he had from ten to twelve movements per day, with agonizing tenesmus and distressful abdominal pains and nausea. For the last month he has ceased to use corn-meal in any form, and the diarrhea has considerably abated. Since December he has lost about 35 pounds in weight, and has been reduced from a robust, virile workingman to a puny, weak, sickly individual, to whom life itself is almost a burden. About ten weeks ago, while picking strawberries, the back of his neck became red and burned as if sunburnt. At the same time he suffered with intense headache, which was confined to the region "behind his ears and extended across from ear to ear." This continued for about ten days. During this period the skin on the back of neck began to peel off. About the same time the skin over the bridge of his nose and the side of his face, after having been red and painful, likewise began to desquamate in small and large dry scales and bran-like particles. About six weeks ago the skin on the back of his hands began to look as if it was blistered, being swollen, red, and painful, and scattered vesicles filled with serous exudates were formed. The surface then became quite dry and hardened, cracking at all joints and between the fingers. Both hands were similarly affected, and about the same extent of surface on each involved. In about a week the skin on the back of the hands, fingers, and lower third of his forearms began to desquamate in the same manner as that on his neck and nose. About the same time all the toes of both feet became swollen and red. They burned slightly and itched

in a most intense manner. This, however, appeared within a week and there was never any induration or desquamation of any portion of the skin. The gums of his upper jaw became swollen and red. There was slight salivation for a few days, but this soon disappeared and has not since recurred. Since December he has vomited only once, that he remembers, but has repeated attacks of nausea every day. During the last ten weeks he has had repeated attacks of vertigo, often becoming dizzy on rising from a sitting to a standing position, or on rising from a recumbent position, and everything becomes black before his eyes.

General Examination.—The patient is a moderately emaciated white man, well advanced in years, with a very apathetic, listless appearance. He answers questions in a slow, whining monotone. He is sitting up, and is able to walk around to a limited extent; however, his gait is slow and he is evidently very weak. He gives a slight groan with each expiration, and appears to be in great distress. His hair is lusterless, dry, and straight. The eyes react sluggishly to light and accommodation. All of the upper teeth have been removed. The lower ones all show more or less marked decay. Pyorrhea alveolaris is quite extensive. Respiration is slightly labored. The skin everywhere has a muddy pallor. The heart, lungs, and thorax show nothing abnormal. The abdomen is scaphoid in shape. The liver, spleen, and kidneys are not palpable. The deep reflexes of the upper and lower extremities are increased. Plantar stimulation gives a slight dorsal flexion of the great toe. No patellar nor ankle clonus can be obtained. There is no Rhomberg's sign, but slight tremor on protruding the

tongue. The patient gives no history of urinary trouble at any period of his life, though for the past four months he has had to get up once or twice every night to micturate; otherwise, negative. Freshly voided urine shows a specific gravity of 1032; deep amber color; sugar and albumin, negative.

Skin.—Over the back of the neck, extending upward to the hair-line and downward to level of upper border of the soft shirt collar, the skin is of a dirty rose-pink color, and everywhere covered with small and medium-sized patches of dry exfoliating epidermis. This superficial epidermis may be easily removed and no bleeding points remain. The same appearance in condition may be noted on each side of the neck, extending as far forward as the anterior border of the sternocleidomastoid muscle. Similar areas over the cheeks, sides and bridge of the nose, and the lateral aspect of the forehead fuse and become continuous with these areas on the neck. The symmetric situation of these lesions on each side of the head is marked. Over each side of nose, especially marked in the region of the alæ nasi, there appears a hypersecretion of the sebaceous glands. The orifices of each gland, filled with grayish-white sebaceous material, gives the skin a white, stippled appearance. The surface of the skin over these areas is quite dry and rough to the touch. In certain places there is a small amount of sebaceous exudate attached to the plaques of dead epidermis, giving them the character of thin crusts. Along the lower areas on the neck and upper margin of the areas on the forehead there is a line of intensified brownish pigmentation. The margins of these roughened areas is everywhere sharp and well defined. Symmetrically situ-



Case of pellagra, showing erratic course of the disease. Patient did not complain of feeling ill. (Courtesy of Dr. J. W. Babcock.)

ated on each side of the neck, just below the lower margin of the roughened area, is a lenticular-shaped area of deeply reddened skin over which the superficial skin appears shriveled. These areas, the patient tells me, have appeared in the last few days, and have the same appearance as the large areas when they were first noticed. The mucous membranes of the lips and conjunctivæ are pale but moist. Skin over the chin and the anterior portion of the neck appears pale and slightly tanned, but otherwise normal. Over the sternum, on the right side, there is a lozenge-shaped area, measuring about 5 by 2 cm.; beginning above at the sternoclavicular articulation, extending downward and inward to the level of the upper border of the third rib, there is a brownish pigmented area of desquamating epidermis. On the left there is a similar area, but smaller. Symmetrically situated on each shoulder, over the acromial process, the spine of the scapula, and the infraspinous fossa, the skin is roughened, harsh, scaly, and covered with numerous patches of brownish, desquamating epidermis. The skin underlying all of these areas is pale, slightly thinned, and very dry and rough. There are also similar areas symmetrically situated over each deltoid and each triceps muscle. The skin over each olecranon process shows the same appearance as that noted above, *i. e.*, a dry, harsh, desquamating superficial skin, and a dry, pale, slightly thinned underlying skin; but after exposure to the sun for a few minutes, as was done when I attempted to photograph the patient's hands, the underlying skin assumed a rose-pink color, similar to that to be described over the hands and arms. The whole surface of both hands, especially the backs of the fingers and hands,

and the lower third of both arms, are everywhere quite rough and scaly. The skin of the dorsum of the hands, wrists, and lower portions of the forearms is of a diffuse erythematous rose-pink color. Scattered over these areas are innumerable small and large patches and plaques of dried and desquamating epidermis. Along all the natural furrows of the hands and wrists, at the interphalangeal joints, and in between the fingers, there are deep cracks. These cracks, the patient tells me, were much deeper a few weeks ago. They were also at that time more painful and tender, and would often bleed after slight injury. Only a few of them now extend through the true skin, and they are all healing rapidly. The skin over the sides of the fingers and the backs of several of the interphalangeal joints is markedly thickened and has the appearance of a saw file. The skin on the palms of the hands is pale, but the superficial layer is dry and harsh to the touch. In places it may be peeled off in large thick plaques, leaving a comparatively normal subjacent skin. The line of separation between the affected and the non-affected skin is sharp and well defined.

Mentality.—The lady of the house tells me that the patient often has fits of extreme irritability, when nothing can be done to please him, and he is extremely fault-finding and quarrelsome. He shows complete orientation, and can remember dates and events accurately, but he has to think over many of them for a considerable time. He can perform simple problems in arithmetic, but with none of the accuracy or rapidity that might be expected of one who had once controlled a business house with a capital stock of five thousand dollars, as he once did, according

to his story. He complains of difficulty in buttoning his shirt and coat, but this is most probably due to the anesthesia produced by the drying and desquamation of the superficial skin over the tips of his fingers.

This word-picture, descriptive of pellagra, as given by Dr. Hewett, is hardly lacking in any detail, showing a careful study of the clinical manifestations and recorded with a care for detail worthy of high commendation. The reader will do well to study it closely.

The next case reported is taken from the description of Dr. Howard Fox, of New York, a patient, formerly under the care of Dr. J. M. Daves, of Blue Ridge, Ga., and seen by Dr. Fox through the influence of Dr. Bernard Wolff, of Atlanta.

This case was also seen by Dr. J. J. Watson and Dr. J. W. Babcock, who both pronounced it a typic case of pellagra of rather a mild type.

Dr. Fox's well-couched description is as follows:

The patient, H. C. H., is a farmer, fifty-one years old, born in Blue Ridge, Fannin County, Ga., where he has lived most of his life. His father died at fifty years of age of an unknown disease. His mother died at sixty-three of the "grip." The patient is the father of thirteen children, eight of whom are living and healthy. Four died as infants. Two of these were twins, two others members of a triple birth. One was born dead at full term. The patient's wife had never had any miscarriages, and had always enjoyed good health. No member of his family had ever suffered from a disease similar to the present one.

The patient had always been a considerable drinker of whisky. He gave no history of syphilis, but admitted

having suffered from an obstinate attack of gonorrhea when about eighteen years old. At twenty-four he suffered from an attack of malaria lasting six months. With the exception of these illnesses he had always enjoyed good health till about two years ago. Since then he had gradually "fallen down" in general health and strength.

The first definite symptoms noted were gradual loss of appetite and an occasional "roaring" in the ears. The latter symptom had been constant for the last ten months. Previous to this time the tinnitus had occurred in attacks lasting a few days.

About the first of April, 1908, the patient noticed a redness and swelling of the backs of the hands, which he at first ascribed to sunburn. The redness was followed by scaling, which lasted for two months. There were a few "blisters" upon the hands at first, but, except at the outset, there were no subjective symptoms whatever. After the disappearance of the eruption the hands looked entirely normal. During the following winter the patient's general health improved.

About the end of March, 1908, an eruption similar to the first appeared on the backs of the hands. This was also followed by scaling several weeks later, leaving the hands smooth, though darker in color. During the past ten months there had been three or four such attacks of redness and scaling on the hands. At no time had the hands become entirely normal. The attacks had appeared in spite of precautions taken by the patient to protect his hands from the sun by wearing gloves and by using bland ointments. There had never been any oozing from the affected area nor had there been any subjective symptoms except,

as before said, at the outset of the attacks. Six months ago there was an eruption of the face and of the dorsal surfaces of the feet somewhat similar to that of the backs of the hands. This has now disappeared, leaving the skin in apparently normal condition.

The patient stated that his tongue had been red during the past summer. According to Dr. Wolff, it presented a fiery-red appearance when seen two months ago. He had not suffered from severe diarrhea except for a short period of a few weeks recently. His bowels have been "more or less loose" during the past summer.

The patient had become more and more depressed since the beginning of his illness and despaired of ever regaining his health. He did not suffer from sudden fits of anger nor excitement. His memory, according to his statement, became very poor.

Examination showed the patient to be a poorly nourished man of medium height. His facial expression was very dull. He was slow in answering questions, his memory was evidently poor, and he was mentally depressed. The pupils were equal, moderately dilated, and reacted normally to light and accommodation. His tongue was slightly redder than normal. The mucous membrane of the lips and mouth were practically normal in appearance.

The backs of the hands presented a symmetric bluish-red area, looking like a fading eczema. This area covered the backs of the wrists, extending slightly around the radial side to the anterior surface. The distal border of the area did not quite extend to the first interphalangeal joints. The skin was smooth and had an atrophied appearance, though to the touch it did not feel very abnormal.

The heart, lungs, and abdominal organs were apparently normal. The pulse was regular in force and frequency, slow, full, and showed marked thickening of the peripheral arteries. There was no tenderness over any portion of the spine. The gait was apparently normal. There was no ataxia. There was some slight rigidity of the muscles of the legs. The patellar reflexes were moderately increased, especially on the left side. There was no ankle-clonus, no Babinski reflex. There were no sensory changes in the skin. The cutaneous reflexes were normal. Examination of the urine showed no abnormal constituents.

An examination of the blood, made by Dr. Elizabeth Finch, was as follows: Hemoglobin (Fleischel), 66 per cent.; red cells, 4,264,000; white cells, 9500. Differential leukocyte count showed polynuclears, 278, 55.6 per cent.; large mononuclears and large lymphocytes (22 transitionals), 16, 38, 7.6 per cent.; small mononuclears and small lymphocytes, 141, 28.3 per cent.; eosinophiles, 37, 7.4 per cent.; mast cells, 6, 1.2 per cent. No nucleated red cells. Red cells pale, but apparently normal in size.

An examination of the nose, throat, and ears, made by Dr. D. Bryson Delavan, showed the following: "Nasopharynx: Typic chronic catarrhal inflammation of the upper nasopharynx and Eustachian tubes, with obstruction of the latter. Ears: Condition appeared to be characteristic of the above. No apparent connection with the general disease."

After this lucid description by Dr. Fox another case will be described, this one by Dr. M. L. Perry, of Parsons, Kansas, and reprinted from the Proceedings of the American Medico-Psychological Association, held at Wash-

ton, May, 1910. Few observers are as able as Dr. Perry to paint the shifting changes in the mentality of these sufferers. His report follows:

I. H., white, female, aged thirty-four, single, no occupation. Admitted to Osawatomie State Hospital 1901, and transferred to Parsons State Hospital 1904. Family history negative. Patient had first convulsion at age of five months, during an attack of cholera infantum. Following this acute illness convulsions continued in a light form, gradually becoming more frequent and severe as she grew older. The first evidence of active mental disturbances at age of fourteen. On admission patient was in vigorous general health, weighing 170 pounds. Feeble-minded, with marked facies epilepticus. She had two short attacks of acute gastritis in the spring of 1908, and severe status in July of same year, otherwise, she remained in good general health until the fall of 1909. A note in the case record, dated June 19, 1909, says, "A big, strong woman, whose health is excellent. Occasionally with a severe seizure she has to go to bed for a day, complaining of feeling nervous and uncomfortable, and does not rest well. Usually is active and a good worker when not cross. Has about fifteen seizures per month. Rather loud and boisterous, but most of the time is good natured, although rough in her manner and language."

In September, 1909, she began to complain of not feeling well, with vague pains in abdomen and lower extremities, anorexia, and some loss of weight. Developed delusions that she had been poisoned, and became depressed, refusing to eat. Was nauseated, and would induce vomiting at times by putting her finger in her throat. Bowels con-

stipated. Tongue furred. Temperature and pulse normal. The sensory symptoms, at first vague and more or less indefinite, soon became very pronounced. Patient complained much of severe pain in abdomen, pelvis, and extremities, and soreness on pressure, and was put to bed.

A note on case record, dated October 18, 1909, says, "Patient has complained recently of severe pain, both on urination and defecation. Examination showed a very fine thick hymen, the opening through which was so small that no vaginal examination was undertaken. The mucous surfaces about the external genitals were somewhat congested and sensitive. Examination of the anus showed a well-marked fissure, with slightly inflamed mucous membrane. The fissure was cauterized with nitrate of silver." Urine was negative. Patellar reflexes abolished, and she soon developed paresthesias in various parts of the body and a marked analgesia in both lower extremities. There was slight fever present, with pulse somewhat weak and accelerated. She had some difficulty in walking, owing to weakness and ataxia in lower limbs. A diagnosis of multiple neuritis was made and patient treated accordingly. There was some improvement observed during the month of November, but a note, dated December 1, 1909, states, "For several days the patient's condition has been more serious, pulse has been hard to count, and general weakness is pronounced. Has been on strychnin, $\frac{1}{30}$ grain every three hours, for two days. To-day was given one pint of water, by rectum, several times with benefit. She has developed a severe stomatitis, which has caused much annoyance." Tongue red and fissured, with small blisters and ulcers around the edge. Mucous membrane on in-

side of the cheeks also showed ulcers. The inflammation extended into the pharynx, making it difficult to swallow solid food. Patient at times refused to eat on account of sore mouth. Temperature ranged from normal to 100.5° F. Bowels still inclined to be constipated, although loose occasionally for a day. She passed small amounts of purulent material. Condition of patient varied somewhat from week to week, but with no marked change until the latter part of January, 1910. She was able to be up and dressed part of the time. The case record shows on January 30, 1910, a sudden rise of temperature to 104° F., following a few days of more sensory complaint than usual. Fever reduced by sponging. At this time she developed an erythema on the dorsum of both hands, particularly marked over the knuckles. The hands in a few days became very rough, with fissures extending through the skin, making open sores in several places. No pain nor itching of hands present, but they were quite sore when handled. The erythema did not extend above the wrist, but there were patches on the elbows. At this time a tentative diagnosis of pellagra was made. Some improvement was observed during the next week, but a note on February 9th says, "During the last few days patient has been very sick, temperature course irregular, much of the time being high, reaching 105° F. on one occasion. She has suffered much from severe vomiting. Treatment symptomatic, cold sponging, strychnin, and nourishment as freely as possible." During these febrile attacks there appeared a pronounced erythema over nose and cheeks, bat-shaped in outline. Later on the skin on both hands and face became scaly, and on the hands much thinned and

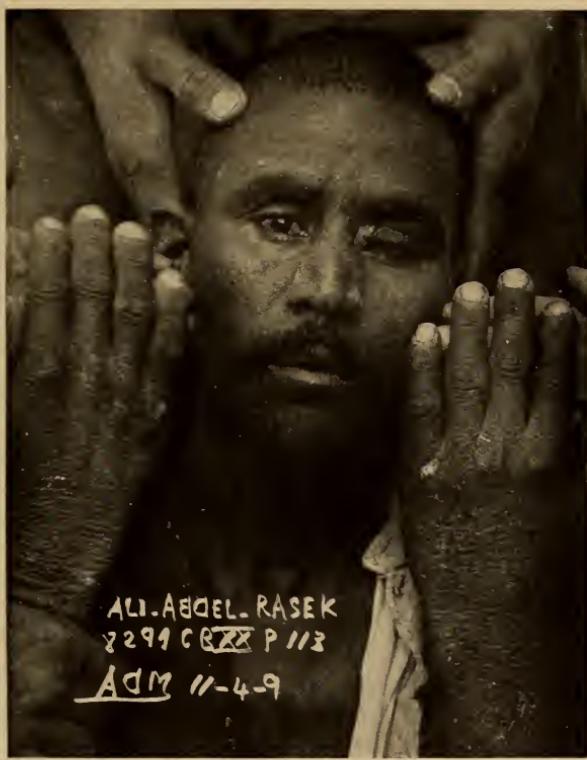
roughened. There was considerable pigmentation, with a quite well-defined line of demarcation at the wrists. Examination of blood-smears showed a reduced number of leukocytes and considerable evidence of anemia.

The mental condition of the patient underwent a very decided change during her last illness. Her emotional state, which had previously been rather exalted, became much depressed, with occasional outbursts of pronounced excitement, the patient being at times kept in bed with extreme difficulty. There was a partial return of the convulsions toward the end of her illness, and a slight tendency to spasticity, but no contractures. Sensory symptoms continued to the end. Died April 16, 1910.

A marked peculiarity of this case is the decided fever at times, so different from the usual afebrile condition of pellagra.

The next report is of an Egyptian pellagrin, under the care of Dr. Warnock, and reported by Dr. Sandwith:

An Egyptian woman, aged twenty-one, was admitted to the asylum on May 15, 1904, with a history of pellagra for the last six months. She was married seven months before admission, but her husband had divorced her because she wandered about for no reason, was sleepless, performed the religious "zikr," talked to herself, and used to fall down when she tried to walk. On admission, she was sleepless, pulse feeble, tongue could not be seen; she had pellagrous rash on her elbows, legs, and trochanters, and her knee-jerks were greatly exaggerated. Her expression was very dull, she complained of being ill in her body, and stated that she was possessed by a devil. On the same day she had a sort of fit, during



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Egyptian case of pellagra. Markedly indurated skin on back of hands.
(Service of Dr. Warnock.)

which the attendant stated that she had contraction of the limbs and head for a short time, but no loss of consciousness. She could walk, but refused to stand up when asked to do so, and was quite demented, forgetful, and unable to converse rationally. She was excited at times, incoherent and noisy, but was able to support herself if she grasped something to pull herself up by. A month later she was still restless, always talking, dirty in her habits, but had no definite delusions. In July she still had staggering gait, was subject to falls, and her muscles were contracted, apparently involuntarily. Her brother, who visited her, said that she had had a black rash on her face and hands that "would not wash off." Her brother denied any syphilis in the family, but had evidently himself suffered from pellagra. In August she was still childish and dirty in her habits, still obliged to catch hold of something to support her when standing up, and her speech was still defective, especially the labial sounds, but she was more cheerful and beginning to put on weight. In November she was fatter, quiet, but still childish, and her speech still defective. She was able to walk and inclined at this time to do some work. She laughed inanely, and volunteered that she had been under sorcery, induced by a man in her village, but the effects had now passed off. In December it was noted, "does some work and has some sense, but is shy and imbecile in demeanor." In January, eight months after admission, she had improved so much that she was able to be discharged, quite strong physically and able to work, but mentally still somewhat childish, thinking she had been under sorcery.

The following case, which came under the care of the

writer, will illustrate the progress of a seemingly rather mild case of pellagra in an aged woman, but which, on account of non-resistance, soon resulted fatally:

Mrs. W. P., aged seventy-one, was seen October 1, 1910, and found to be a slender and fragile woman, looking fully her age. She was referred by another physician, who had noted a rough, scaly appearance of both hands, extending up both forearms like a gauntlet.

Her past history was not productive of interest, except that she reported a "spring feeling," as she termed it, for the past three years, during which time, for about two months in the early summer, she suffered from lassitude and slight diarrhea. For this she had gone to the mountains, each time seeming to obtain relief and strength. Being in comfortable financial circumstances, she had been able to take every care of herself, and attributed the diarrhea to dietetic indiscretions; the slight erythema she thought was caused by exposure to sun and wind during her tramps in the mountains.

Upon physical examination, her heart was found to be normal, though the second sound was not very sharp; her lungs were normal; her arteries were somewhat sclerosed, but her blood-pressure was not high. The arcus senilis was most distinct in her eyes. Her stomach was normal in size, but ptosed about two inches. Her abdominal walls were extremely thin, permitting the peristalsis of the intestines to be plainly seen. Her muscular system was flabby, her limbs were wobbly, and her hands tremulous. Her voice was quavering and uncertain. There were no dermal lesions except on her hands and forearms, these showing a rather faded erythema. Her tongue showed

a surface denuded of epithelium around the edges, and was pale and tremulous. She did not complain of her tongue being sore, but said her taste was not discriminating as it had formerly been. At present everything tasted the same to her.

Her appetite was poor, her food seemed to "lie heavily" in her stomach for several hours after eating, and articles that formerly agreed with her seemed to nauseate and distress her. Her bowels were loose, moving four or five times daily, preceded by colicky pains, the movements frothy and foul smelling. She also noted a great difficulty in controlling her anal sphincters, on several occasions having soiled her linen before she could get to the toilet. She admitted being more forgetful than usual, but her husband remarked on her seeming decline in mentality, for she had been a woman of fine force of character.

Treatment seemed at first to aid her, but not for long. Her hands began to desquamate, appearing for a time as if they were improving, but it was soon noted that the skin under the desquamated epidermis seemed to desiccate and become rough as soon as it was exposed. Her general complexion, too, became ashy, her skin taking on a harsh and wrinkled appearance. Her diarrhea remained about the same, though by October 20th at least half of her movements were involuntary. Her appetite diminished from day to day, so that it was with the utmost difficulty that she could be induced to partake of any food at all. This disinclination to eat arose both from anorexia and a sitophobia, for she feared the distress that followed each meal. Her mouth began to be somewhat sore, and the mucous membranes of her lips, before pale, now became a cherry

red. With failing bodily strength came weakened mentality, and in a dreamy, aimless way she would answer questions or make requests pertaining to her comfort. During her illness the temperature was never over 98° F., and generally about 97° F.

With a steady downward course she declined, complaining but little, and scarcely seeming to realize that she was ill. During the last five days of her life, she was semi-comatose, her bowels moved involuntarily, her reflexes were abolished, dysphagia was marked, her pulse was slow and feeble, and she succumbed with hardly a struggle on November 12th.

Had this patient been young and resistant, the disease would have probably assumed an entirely different aspect.

To show how widely variant pellagra may appear, one more case, this, too, under the observation of the writer, will be cited. As in the first, the whole picture was one of weakness and non-resistance, the second will show a sthenic form of pellagra, in which a vigorous vitality seems to have conquered.

The patient, Miss A., twenty-four years old, previous health good, was seen in July, 1911, in an apparently precarious condition with pellagra. She had lost a younger sister two months previously with this disease, the fatal result having occurred in the second recurrence. The rest of the family were well, and both parents seemed free from any pellagrous taint.

She had always been a healthy, though rather nervous, girl, and in the spring of 1910 she suffered from "diarrhea with sunburned hands." The diarrhea, as has so often



Author's case of pellagra. Patient seems to have recovered.

been the case, was ascribed to errors in diet, and the sunburn to exposure. This seemingly slight indisposition disappeared during the summer, and throughout the fall and winter she enjoyed her usual health.

In March, 1911, the diarrhea and erythema reappeared, and with the added impression of her sister's illness, being much like hers, she began to grow melancholy and apprehensive of dire results. She continued to grow worse, both as to the gastro-intestinal symptoms and the erythema, the latter showing in symmetric patches on her face, neck, breast, and lower limbs. During this time also her parents were much troubled by her frequent emotional outbursts, and, when the other sister unexpectedly died, they and she woke up to the gravity of the situation.

She was sent to several resorts in the hope of restoration to health, but she steadily declined until she was brought to Atlanta for treatment.

When seen by the writer she presented a melancholy picture. The erythema was quite extensive in some places, mostly on the nose, forehead, and neck, having assumed a dingy hue, while the palmar and plantar surfaces had become a distinct black, showing an inclination to peel off in several places. In several of the interphalangeal spaces cracks had formed from which exuded much serum. Her tongue, lips, and buccal surfaces were absolutely raw, also the vulvovaginal margins and the anal margins. A sero-sanguinolent discharge from the irritated vagina and anus kept the inner aspect of the thighs and buttocks almost raw, while the relaxed and incompetent anal sphincters permitted the watery feces to spurt out at frequent intervals.

Mentally she was in fully as pitiable a state. A dreamy delirium, broken only by horrid dreams and phobias, was present, out of which she was aroused with difficulty. The reflexes were much exaggerated. Occasionally, when she showed lucid intervals, she complained of numbness and formication, and was fearful that her heart would suddenly stop beating.

Her temperature for two weeks seldom ran under 100° F. in the mornings, sometimes going up as high as 104° F. in the evenings.

Under energetic treatment she began, in about two weeks, to show signs of improvement, practically all of her symptoms showing the same uplift. As her bowels improved, so did her mind and her erythema, while her sore tongue and mouth rapidly lost their fiery red and raw appearance. The dry and rough skin peeled off in great flakes, leaving a pink and exceedingly tender surface. Her feces assumed a semisolid consistency, though she still had to be quite careful to promptly evacuate her bowels when the desire manifested itself, or she would soil her linen.

Her mind also became clear, but she was somewhat emotional and easily excited to tears.

This young patient was in September able to return home, and at present is reported as apparently well. Whether this improvement will or will not be permanent, time alone will tell.

The description of these several cases in widely scattered localities covers pellagra in its major and plainer forms. The many variations, the many deviations from the classic picture, the many atypic or complicated cases, will have to be recognized and treated on their merits.

It behooves the thoughtful reader to scan with discriminating care the many shades of bodily and psychic deviations from the normal as set forth here, and the way will be paved for a better understanding of the chapter on Diagnosis and Prognosis.

CHAPTER VI

PATHOLOGY AND MORBID ANATOMY OF PELLAGRA

THE morbid anatomy of pellagra is neither constant nor characteristic. The chronicity of the disease, the variety of symptoms, the many complications and intercurrent affections, preclude the naming of any single definite set of changes as belonging to its pathology.

Tuczek, as quoted by Lavinder, described as part appearances of cachexia the following: Wasting of adipose and muscular tissues, brittleness of the bones (*fragilitas ossium*), atrophy and fatty degenerations of the internal organs (chiefly those innervated by the vagus), heart, kidneys, spleen, intestines, liver, and lungs.

He also describes three further groups of morbid changes: (1) Intestinal—atrophy of muscular coat, with occasional hyperemia and ulceration of the lower part of the tract; (2) abnormal pigmentation (similar to senile change), especially of ganglionic cells, heart musculature (brown atrophy), hepatic cells, and spleen; (3) ulcerations in the nervous system. The variously described conditions of hyperemia, anemia, edema, and at times inflammatory affections of the central nervous system and its coverings, together with the obliteration of the central canal of the cord, he regards as not peculiar to pellagra, but as ac-

companying conditions, present in many chronic affections of the central nervous system and in senility.

The findings in the brain are in most cases negative, except for occasional fatty degeneration or calcification of the intima of small blood-vessels and pigmentation in the adventitial coats. In cases where a long-continued psychosis had led to a high degree of imbecility, atrophy of the cerebrum may be found. In the cord the changes are fairly constant and important: degenerations in the lateral columns in the dorsal region, and in the posterior columns in the cervical and dorsal regions; very few changes are found in the lumbar cord.

Summarizing the data obtained from 153 examinations of the cerebrospinal fluid of 106 cases of pellagra, W. F. Lorenz, Special Expert, U. S. Public Health Service, reports as follows:

(1) A lymphocytosis of the cerebral fluid does not occur in uncomplicated pellagra.

(2) Globulin excess of the spinal fluid is only occasionally observed.

(3) Lange's colloidal gold chlorid test is uniformly negative in pellagra.

(4) The Wassermann is negative with a few exceptions. In this investigation the exceptions were moribund cases which gave weakly positive reactions with blood-serum.

(5) The spinal fluid findings would seem inconsistent with a conception that pellagra is an infectious disease of the central nervous system. (Public Health Reports. Reprint 218.)

In autopsies performed by Dr. Sandwith, he noted great emaciation and cachexia, generally with marked anemia.

There may be definite exfoliating patches on the parts of the body exposed to the sun during life, or there may be only a little roughness of these parts, but the skin there, if carefully examined, will be found to be atrophied, and there is a general diminution of subcutaneous fat. Microscopically, there is sclerosis of the blood-vessels, papillæ, and corium, as well as atrophy of the horny layer.

The muscles, heart, liver, kidneys, and spleen share in the general atrophy.

The lungs sometimes show tubercular lesions. The stomach reveals no lesion to the eye, but the walls of the intestines are thinner than usual, and show a slight shedding of the superficial layers of the epithelium, with atrophy of the muscular tissue. There is no ulceration of the intestines. Many naked-eye lesions have been reported by various observers as occurring in the brain, but the only constant one is atrophy of the cortex of the convolutions, especially the frontal.

Dr. Sandwith took from Egypt to England two brains, which Dr. Mott examined for him, though they did not arrive in a satisfactory condition. There were, however, found in them evidences of chronic slight but diffuse meningomyelitis.

Dr. Mott found no decided changes in the spinal cord until it was prepared and carefully examined. Tuczek, though, in 1893, found in 8 autopsies in Italy that all of them showed symmetric sclerosis of the columns of Goll. In 6 cases, also, there was lateral sclerosis in the dorsal region, and in 1 case he found cervical anterior sclerosis.

In 1899 Dr. E. F. Batten made, for Dr. Sandwith, many

sections of three pellagrous cords, and furnished the following report on them:

Marchi's Method.—The paleness of the posterior columns was very noticeable, but under the microscope no recently degenerate fibers could be seen. The cells of the anterior horns were pigmented.

Weigert-Pal Method.—The lack of fibers in the posterior columns was very marked, both sacral and lumbar regions being affected equally. In the mid-dorsal region a pair of normal roots entered the cord, and wedged itself in between the atrophied fibers of the median and external columns; this root could be traced up to the upper cervical region, where, again, the incoming roots contained more normal fiber. A small wedge-shaped tract was also visible just outside the anterior horns of the cervical region.

Aniline-blue-black Method.—The increase of the connective tissue in the posterior columns was very marked, and distributed itself in exact correspondence with the condition of the roots above described, namely, a pair of roots, which had undergone no degeneration in the dorsal region, showed no increase of the connective tissue in the area it occupied in the cord. There was no increased vascularity of the cord, the cells of the anterior horn and the nucleus and nucleolus were distinct, the increase of the connective tissue was limited to the posterior columns, except in the wedge-shaped tract above described in the cervical region, which appeared darker owing to the smallness of the film in this area.

Van Giesen's Method.—There was no evidence of any recent inflammatory action in the gray matter. There was some thickening of the walls of the smaller vessels, espe-

cially in the posterior columns, though it was not limited to this region.

The posterior roots of the cervical, dorsal, and lumbar regions were also examined in this case by Marchi, Weigert-Pal, and Strobe's methods. Marchi's method showed very little recent degeneration, though it was obvious, from the lack of staining, that a very considerable amount of degeneration had taken place, and this was made evident by staining by the Weigert-Pal method. The greatest amount of destruction seemed to have taken place in the dorsal and lumbar regions, and to a lesser extent in the cervical region; the same condition was also shown by the Strobe stain; only a few axis-cylinders could be seen in each root.

This patient died of pellagra and chronic kidney disease, but there was no possibility of knowing how many years she had suffered from pellagra.

According to Dr. Sandwith's opinion the cord degeneration would appear to be of root origin, and affects the extramedullary as well as the intramedullary portion of the posterior roots. The degeneration in the cervical region of this cord was most marked in the columns of Goll, the columns of Burdach being affected to a lesser degree. Since then he has had many other sections cut and examined by experts, but, unfortunately, nothing of pathologic interest was revealed. The absence of cord degeneration in these cases was due to the fact that the patients had either had pellagra for too short a time—one year or less—or that, though they had suffered from pellagra for three years or more, the clinical signs of the disease were not very far advanced. In other words, spinal cord degenera-

tion, as discovered by the microscope, is a comparatively late lesion in the disease.

The following remarks from a recent paper of Dr. J. D. Long show his views as to certain pathologic lesions in pellagra:

"As to the lesions on various parts of the body, in every case of pellagra in which radiographs were made the plates showed deposits in the spinal foraminae which apparently produced pressure on the nerves. As to the part played by toxic degeneration of the nerves themselves, I can only repeat what I was told by Dr. Achucaro, of the Government Hospital for the Insane, Washington, D. C., that experiments show, when various tissues, such as nerves, muscle, and fat, are allowed to decompose, that the nerve, being the most highly specialized of all the tissues, shows evidences of degeneration first.

"It is possible that several factors may be concerned in the seasonal recurrence of the disease: first, renewed activity and renewed infections with amebæ in the spring of the year; second, engorgement of the intestines, due to chilling of the body surface; third, the growth of molds in food products, with resulting changes in these products, which could favor fermentation in a person already debilitated.

"As to the degeneration of the posterolateral columns of the spinal cord, Marie made the observation that the degeneration began in the posterior of the spinal nerves. The radiographs showed that the pressure does come on the posterior roots of these nerves at about the site of the ganglion. Further, at the only autopsy I could obtain, it was noticed that the foramina were so filled with what

seemed to be a firm cartilage-like deposit that the nerves were wedged therein, and a large-sized sewing-needle or a Japanese tooth-pick could not be pushed through the foramina. The spinal canal was also partially filled.

"It may be seen from the skeleton and the radiographs that the foramina in the cervical region decrease in size from above downward, whereas the nerves increase. These facts would seem to account for the lesions on the hands (fifth, sixth, seventh, eighth cervical, and first dorsal), face, and neck (third and fourth cervical).

"With reference to the dorsal nerves, Gray says, 'The roots of the dorsal nerves are of small size, and vary but slightly from the second to the last.' Examination of the skeleton shows these foramina to be larger than the lower cervical, and, therefore, there are no lesions on the parts innervated by the dorsal nerves.

"The lesions on the legs and feet are due to pressure on the first and second sacral nerves, of which Gray says, 'The roots of the upper sacral nerves are the largest of all the spinal nerves, while those of the lowest sacral and coccygeal nerves are the smallest.' The foramina are larger than the other intervertebral foramina, but are more tortuous, and, as the spinal canal in the sacrum is incomplete posteriorly and flattened, it is possible that any deposit here will produce pressure-symptoms as in the other vertebræ."

Dr. J. C. Bardin, pathologist of the Central State Hospital, Petersburg, Va., has recently made postmortems on 5 cases of pellagra, and has carefully investigated the blood in 14. He has rendered a most interesting account of his findings in the October issue of the American

Journal of Insanity, and the following are abstracts of his article:

He considers that pellagrins are specially prone to contract tuberculosis—particularly intestinal tuberculosis—and seem to be an easy prey to intestinal parasites at nearly every stage of the disease. The pellagrous lesions of the intestines naturally render them more vulnerable to any organism that might happen to enter. Dr. Bardin opines that cases of intestinal tuberculosis occurring in patients suffering with pellagra cannot be detected, save in rare instances, until postmortem is done.

In the American Journal of Insanity, July, 1913, Dr. Bardin commented on the marked eosinophilia in pellagrins infected with intestinal parasites, which, however, does not affect the lymphocyte counts. He further remarks: "One who has not observed the feces of negroes can have no idea how heavily they are sometimes infected with these organisms; and it is to be wondered at that more of our cases of pellagra do not show this condition."

Were it possible to give a definite sequence of temperature to pellagra, so that it could be differentiated from tuberculosis, it would be possible, by keeping charts of all patients in the diarrheal period, to detect those complicated by tuberculosis of the bowel. Unfortunately this has not been practicable.

Three out of the 5 cases examined postmortem showed tuberculosis of the bowel, and a fourth showed healed lesions of the lungs. Another case, that did not die, was diagnosed tuberculosis of the lungs, and was sent to a tuberculosis colony. While recovering from tuberculosis, pellagra developed. This patient went through a typic attack of

pellagra, but both the pellagra and tuberculosis improved during the same time, and the recovery from both seemed complete.

The writer does not doubt that tuberculosis complicates many of these pellagrous cases, especially those with persistent diarrhea. In analyzing the findings in 14 cases, considerable discrepancy was found to exist between the blood of those pellagrins having tuberculosis and those not having it. The discrepancies occurred principally in the differential leukocyte counts.

The blood examinations were made by Dr. Bardin, as far as possible, while the pellagrous symptoms were at their height—that is, when there was marked diarrhea, erythema, and stomatitis. In making the red and white counts the usual technic was employed, and at least six different fields were counted and averaged in each examination. A variation of six leukocytes was allowed between the highest and lowest field counts. At least four white counts were made in each case and the results averaged.

The results of the several tables gotten up by Dr. Bardin show that there is usually a well-marked reduction in the number of red blood-cells, a diminution in the percentage of hemoglobin, and but little change in the leukocytes in all the cases.

The differential counts show a variable reduction in the percentage of polymorphonuclears; a marked variability in the percentage of small lymphocytes; a fairly constant, but small increase in large lymphocytes; and a marked diminution in eosinophiles.

Leaving out some interesting tables showing the blood-

counts in cases complicated by tuberculosis, we find that Dr. Bardin observed that in uncomplicated pellagra the small lymphocytes seem to be increased in proportion to the severity of the skin lesions, though this does not always hold good. He has also observed that the more chronic the case, the more small lymphocytes there will be relatively. He has been struck with one or two things in cases of uncomplicated pellagra that occur with too great a regularity to be accidental. They are an increase in lymphocytes, with a corresponding reduction in polymorphonuclears and a marked reduction in eosinophiles. These variations from the normal blood-picture seem fairly constant. Further than this Dr. Bardin does not commit himself.

The studies of the cytology of the blood by Drs. O. S. Hillman and P. A. Schule have not disclosed any constant abnormality. A lymphocytosis was observed in approximately 75 per cent. of the cases examined by them.

The writer is able to obtain a personal report from Dr. E. C. Thrash, of Atlanta, who has recently held four postmortems on pellagrins whose illness has lasted a variable length of time. As a result of these postmortems he has formed certain conclusions embodied herein. The result of all profound anemias is a cloudy swelling of the cell structures of the various organs of the body with other atrophies. This is so not only of toxic conditions resulting from poisons emanating from organic living matter, but also from chemical poisons. There is no exception to this rule in pellagra.

In the more acute cases there is hyperemia and cell migration in the brain, liver, spleen, and kidneys. In

those assuming a chronic condition there are atrophic changes that simulate those changes which take place following albuminous degeneration of cell structures resulting from other toxemias, which are complete atrophy, vacuolization, degeneration of the nucleus characterized by failure to take the basic stains, infiltration of pigment (brown atrophy), and abiotrophy or partial death of the cells.

The brain especially shows this condition, there being cell degenerations in the cortical structure of the brain and lateral and posterior columns of the cord, the cell degenerations here mentioned. When the nobler cells are degenerated or completely destroyed, there is infiltration of connective-tissue stroma to supply the void caused by the death of these cells. This accounts for the excessive amount of neuroglia tissues found in the cortical structure of the brain, and especially in the lateral and posterior columns, causing the pathologic findings in this disease to simulate locomotor ataxia. This same degenerative process takes place not only in the brain, but in the kidneys, liver, spleen, and, in a measure, the muscular structures, especially the heart, as in one case there was a brown atrophy of the heart musculature much simulating senility.

Intestines.—In two of these cases examined the intestines showed conditions which were somewhat different from reports ordinarily given in postmortem findings. There was no ulceration and but little change in the appearance of the intestinal mucosa, except a decided thickening of the intestinal walls in certain areas. The microscopic examination showed that this thickening was due to

an infiltration of fibrous tissue, the musculature having almost entirely disappeared. The mucosa showed but little change except that of chronic inflammation characterized by atrophy and disappearance of some of the columnar cells, and infiltration of connective-tissue stroma, which stroma had numbers of foci of amyloid degeneration. Whether this was a terminal condition resulting from long-continued illness and cachexia which might have appeared in other diseases, Dr. Thrash could not say. His observation and findings led him to believe that the intestinal and stomach disturbances in pellagra are secondary, resulting from nature's effort to be relieved of poisonings which have been ingested, and which have resulted from perverted metabolism and various atrophic changes of all the cell structures of the body.

This condition must be relieved by the emunctory organs, and they, suffering from the changes mentioned, must naturally be unable to perform their function, and necessarily the alimentary tract would have extra demands made upon it, which brings on the train of symptoms with which we are so familiar.

Since the first edition of this book was published, Dr. Thrash, in his postmortem work at Grady Hospital, has performed a number of autopsies on pellagrins, and his later findings present no notable additions to his previous report.

Passing on to some of the special organs, we note certain morbid conditions obtaining in most cases of pellagra, though not invariably, and some of these changes are found nearly, if not fully, as often in some other diseases.

In Lombardy, edema of the lungs, pleurisy, hyperemia,

emphysema, and pneumonia were frequently found in conjunction with pellagra. Tuberculosis was rare, though there may have been some local reason for this. With us, in this country, tuberculosis in pellagrins is not uncommon.

In many autopsies brown atrophy of the heart muscle has been observed, also frequent softening of the myocardium. Apart from this, no special pellagrous lesions of the heart have been found.

Lesions of the liver are rather common. Sometimes it is small, sometimes it is large and friable, and brown atrophy occurs. In 29 autopsies made in Italy there were 7 cirrhoses and 9 fatty livers. Sometimes the weight of the liver is diminished by half. Fatty infiltration is often found, and congestion or granulofatty degeneration.

The spleen is often atrophied, occasionally hypertrophied. There have been atrophied spleens noted even in typhoid pellagra.

Seldom are normal kidneys found in pellagrins. They may be fatty, atrophied, cirrhotic, or cystic. In over half of the cases the weight of the kidneys is diminished. Often asymmetric renal sclerosis is present, and fatty degeneration of the epithelium of the tubules is found, with or without interstitial sclerosis.

Fragility of the bones of the skeleton has been noted by several observers. This fragility is supposed to depend on the eccentric atrophy of the compact substance with hypertrophy of the medullary substances, and has been seemingly demonstrated by the microscope.

The main skin lesions, as described by Griffini, consist of marked atrophy of the stratum corneum, copious desquama-

tion, active reproduction in the Malpighian reticulum, and marked sclerosis of the vessels of the papillary layer and the derma.

Pigmentary degenerations are frequent, some of which have been already noted. There may be found brown atrophy of the heart, pigmentation of the liver cells, pigmentation of the cerebral vessels and of the spinal and ganglionic cells. In one case there was observed a general pigmentation of the kidneys, heart, liver, and the vessels of the brain.

The calcareous degeneration of the cerebral vessels, the thickening of the membranes of the brain and of its vessels, help to explain the frequent psychic disorders which almost invariably accompany pellagra.

Also, as was noted by Dr. Thrash, the tendency to atheroma and precocious senility is one of the most remarkable and frequent pathologic changes in pellagra.

The pathology has by no means been worked out to any definite status in pellagra, and the writer has been forced to gather to the best advantage the sometimes divergent views of different observers.

CHAPTER VII

DIAGNOSIS, COURSE AND PROGRESS, AND PROGNOSIS OF PELLAGRA

DIAGNOSIS

AFTER so much has been written concerning the clinical history and symptomatology of pellagra, it might be surmised that to diagnosticate this malady would be an easy matter. This is so in typic manifestation, as it is in typic manifestations of any other disease entity.

To one who has mastered the rudiments of diagnosis and symptomatology, such diseases as variola, measles, pertussis, and others that might be mentioned, would offer no difficulty were their pathognomonic symptoms squarely and openly exhibited.

Thus, with pellagra, when the erythema, the diarrhea, the depressed mentality, and the nerve pains all come together, the diagnosis is thrust on the physician *nolens volens*. The very many atypic cases, however, that are constantly cropping up, together with the great importance to the patient of an early diagnosis, make it highly essential that as clear a diagnostic picture as can be possibly drawn should be presented to the student of this oftentimes puzzling and perplexing malady.

Viewing it in perspective, we might say that pellagra presented a fourfold syndrome, the presence of at least two

units of which would be necessary in order to make a diagnosis. Ofttimes two are not quite sufficient for a positive diagnosis, though they furnish reasonable certainty, and a tentative diagnosis is justified. Three of the group would make out quite a strong case, while all four being present would render the diagnosis an absolute certainty.

According to the views of the writer, who has given the diagnosis much thought, it is most practicable to divide this fourfold diagnostic syndrome into the aspects of *gastro-intestinal*, *dermal*, *nervous*, and *psychic*.

It should be remembered that there is no definite rule as to the appearance of any one of these factors at any specific stage of the disease. For instance, there may have been vague gastro-intestinal disturbances, intermittent in character and punctuated by periods of seemingly perfect health. Some of these patients may have suffered from digestive ailments irrespective of the pellagrous onset for a number of years, so that the gastro-intestinal symptoms may seem but an exacerbation of the original chronic trouble.

In a not inconsiderable number of well-developed cases of pellagra, if care is taken to bring it out, a history of slight, almost ephemeral, "sunburns," occurring in previous springs or summers, and occasioning neither discomfort nor anxiety, may be elicited. In many pellagrins, who perform manual labor, men who work in the open, who are exposed to the vicissitudes of the weather, or who handle heavy burdens; women who perform laborious household duties, who scrub, wash dishes and clothes, whose hands are much in hot water, and whose busy feet can hardly keep pace with the constant demands, these pay but scant

attention to slight erythemas, dismissing them with hardly a passing thought.

Again, the dermal manifestations are occasionally *late* symptoms, preceded by one or more of the other factors, and only needed to "clinch" the diagnosis. However, to wait for these might cause the patient to lose precious time—time which might spell the difference between recovery and death.

The manifold symptoms of nerve-irritation, appearing in such varied guises, may be easily mistaken for many pathologic conditions. The lightning pains of tabes dorsalis; the disquieting pangs of an incipient sciatica; the reflex neuralgias from previous inflammatory lesions; the nervous rumblings from an ancient gumma, which perhaps has reposed in a state of "innocuous desuetude" for years—such as these may mask the nervous picture, and also cause a loss of valuable time.

In the psychic factor of the syndrome, the actual beginning of the deviation from normal is probably the most difficult of all. To fairly judge temperamental changes; to estimate slight lapses of mental poise; to differentiate between a dissatisfaction or a slight delusion, or between a real dislike or an obsession of distrust; to estimate the various grades of unhappiness, extending from hardly realized mental depression to deep melancholia or positive forms of insanity—these, too, will tax to the uttermost the skill and acumen of the conscientious student of this disease.

Another caution may appropriately be given in regard to making diagnosis of pellagra on insufficient evidence.

When several cases have appeared in some community,

and rumors as to its spread are rife, there is sometimes a tendency to diagnose certain illnesses as pellagra, when a more careful analysis would have shown the obvious errors.

Within the last six months the writer has seen diagnosed as pellagra such troubles as pyorrhea alveolaris, with sore gums and irritated tongue, but not another pellagrous symptom; tuberculosis of the intestines, with chronic diarrhea, but no erythema or psychasthenia; aphthous stomatitis; marasmus with profound anemia; simple melancholia; and one case of acute mania, where there was absolutely no excuse for such a mistake. In the last-mentioned instance the patient, a woman, became suddenly and wildly unbalanced mentally. There was no diarrhea, no history of indigestion, no erythema—nothing but a disturbed mentality, which was manifested by a violent delirium, and which later on ended in recovery.

To diagnose such cases as pellagra, with all that this diagnosis entails, is unjust to the patient, and liable to reflect seriously on the attending physician's judgment.

When a suspected case of pellagra presents itself, the history should be carefully taken and the following points noted:

Has there been a history of indigestion at irregular intervals without apparent cause? Have certain articles recently disagreed that formerly agreed with the patient? Has the patient suffered with anorexia, or colicky pains, or diarrhea, or tenesmus? Have there been vague or active neuralgic pains, or has there been burning of the hands, feet, tongue, or buccal membranes? These symptoms, if present, are exceedingly suspicious. Has there been a sense of malaise or weakness in the preceding spring, or

any previous springs or other seasons of the year? If this malaise has been present in the spring or summer, has it cleared up in the fall and winter? Has there been any "sunburn" of the hands or face or neck, or has there been any "chapped" hands or lips, which later on seemed well, but left for a while a tender pink surface? Has the tongue been sore, or have there been any "mouth ulcers" or sore lips or cheeks? Have there been any spells of "blues" or periods when it seemed everything went wrong? Another question, to which the *patient* cannot give a correct answer, is regarding any change of disposition or feeling toward those near and dear. It has been often found in the mental perversion of pellagra that antipathies would spring up against those closest by ties of blood and companionship.

Has there been insomnia, followed by an intense melancholy? Has fear of impending danger or a vague, undefined sense of ill-being brought about unhappy days and "nights devoid of ease"? Has the disposition seemed to undergo a transformation, so that a formerly cheerful temperament has lapsed into an unhappy and morose personality? These and others of like import are needed to bring out the salient points in the diagnosis of pellagra.

The following combined symptoms are strongly indicative of a positive diagnosis of this disease:

A symmetric erythema of either the hands, forearms, sides of neck (rarely), sides of nose (rarely), sides of forehead (rarely), or the dorsal surfaces of both feet. The writer recalls no case of pellagra presenting a one-sided skin lesion. This erythema may be only a decided blush, not extending below the epidermis, but it must be symmetric,

scaly, rather rough, and present a distinct line of demarcation at the junction with the healthy skin. Should the erythema be more pronounced, showing the surface of a dull pink, as if it had been "baked in a stove," should the dorsal surfaces of the hands appear rather "shiny," possibly merging into cracked and tender interphalangeal spaces, with dry, rough and scaly feel, and dingy brown or black palmar surfaces, this would constitute a formidable link in the chain of evidence. The erythematous patches on other parts of the body are not pathognomonic unless in conjunction with the others mentioned.

Should there be in addition to this erythema, a sore tongue or mouth, cherry-red and tender lips, inflamed buccal surfaces; tongue red and inflamed on the top or around the edges and denuded of epithelium, aphthous ulcers on the tongue or in the buccal cavity, with dysphagia either from soreness or "nervousness," this makes still stronger the first link in the chain.

Next come the gastro-intestinal symptoms, to which attention has been called. Should the patient complain of indigestion, to which is added colicky pains, and especially a diarrhea, apparently causeless, spasmodic, tending to involuntary evacuations, but little affected by what is eaten and exceedingly foul, another link has been added to the pellagrous bill of indictment.

If, in addition to the other symptoms, the patient should complain of shooting pains in the head or limbs; of paresthesias, or formications, of anesthetic or hyperesthetic areas; of intense burning of the mouth, tongue, hands or feet, or any other part of the body; if the locomotion was unsteady or impaired; if tremor appeared in the hands or

tongue; if there are dizziness with the eyes closed or fear of walking in the dark on account of pedal anesthesia, still another link is added.

If, in corroboration of the previous symptoms, there is more or less mental depression, verging into melancholy, or deeper forms of psychic abnormality; if the temperament has undergone a decided change; if there are doubts, fears, or obsessions where there were formerly courage, fortitude, and a clear vision of men and affairs; finally, if mental failure goes apace with bodily cachexia, the picture may be considered complete, the links in the chain of pellagrous evidence uninterrupted, doubts may be cast aside, and the diagnosis may be made with entire assurance.

Where two factors in this syndrome are plainly manifested, it is sometimes perfectly safe to make a diagnosis of pellagra; for instance, if there is the characteristic erythema, coupled with an indigestion and diarrhea. The nervous and mental symptoms may be absent, but the other evidence may be sufficient. Again, there may be present a sore mouth and tongue, presenting the pellagrous appearance, and there may be diarrhea and gastric distress in evidence. In such an instance, while the presumptive evidence is strong enough to warrant putting the patient under treatment for pellagra, it would hardly be safe to make a positive diagnosis unless either the erythema or nervous or mental symptoms entered in evidence.

The writer recently diagnosed a case upon the evidence of slight nervousness and a mild erythema. The other symptoms were absolutely lacking, but the erythema was so symmetric and characteristic that no doubt was enter-

tained as to other symptoms showing up later on. This expectation was realized about two months later, when a colicky diarrhea set in.

Whether or not a physician is justified in making a diagnosis of pellagra when there are at no times in the course of the illness any eruption, is an open question. "*Pellagra sine pellagra*" is a term that is odious to some, impossible to others, and ridiculous to a few. The writer feels that it is possible for a case to run a certain course without any eruption, but he would be exceedingly chary in diagnostinating such a manifestation unless the other *three* factors in the fourfold syndromes were present beyond a peradventure.

Scurvy, leprosy, beriberi, and syphilis have been mistaken for pellagra, but should be easily differentiated, if care is taken.

Chronic mercurial and arsenic poisoning should show but little difficulty in elimination from a pellagrous diagnosis.

Some food or occupation poisonings need occasionally to be differentiated, but the development is generally different and the pellagrous syndrome is incomplete.

Occasionally, when the disease assumes a typhoid character rather early in its course, it is possible to confound it with one of the infectious diseases, but proper analytic precautions will generally suffice to clear up the diagnosis.

This presentation of the diagnostic syndrome, together with the other aids, as previously laid down, is thought by the writer to be full enough to enable any thoughtful observer to recognize pellagra.

COURSE OF THE DISEASE

A part of this has been already covered in previous chapters, but some of the features require additional discussion.

Pellagra is essentially a *chronic* disease, and in minor degrees may lurk in the system for many years. One writer has expressed the belief that some cases have lain latent for as long as thirty years, only to take on an added pathologic impetus, rapidly proving fatal. Many are the reports of cases lasting five, ten, or fifteen years, where the recurrences are *unmistakable*. These intermittent pellagras in robust persons, where the habits are good and the environment favorable, may run an almost indefinite course, permitting the sufferer to die of some other ailment.

In the majority of cases the first manifestation of any sort appears in the spring of the year, and either disappears by summer or fall, or decreases in severity. In this apparently prodromal stage the physician is seldom consulted, or if so, is generally consulted for some other supposed illness.

Should there be any eruption, it is, as stated, ascribed to other causes.

The writer agrees with Dr. Harris, in part, as to many cases of chronic "dyspepsia," diarrhea, or obscure debility that have come on from year to year, not quite making an invalid of the sufferer, but preventing a full adaptation to all the requirements of active life, being, in reality, instances of "corn-bread poisoning."

In the opinion of most of the students of pellagra, it is never fatal in its first appearance, and will either intermit or remit of its own accord.

It is in the second, third, or later recrudescence that the toxin seems to have gained a sufficient momentum, as it were, to wreak serious damages. It is then that the different factors in the syndrome begin to assemble, and the picture of pellagra begins to assume pathologic shape.

Pellagra seems essentially a disease of hot weather. While not all the deaths from this cause occur during the heated term, the vast majority do, and those who have had experience know full well how all the symptoms of improvement are hastened with the advent of cold weather, and even the fulminant cases seemingly halted in their progress toward a fatal termination. There are, of course, exceptions to this, but they are few—not more than the exceptions in other chronic seasonal diseases.

Having passed the incubative stage, or the prodromal stage, or pellagra of the first degree, as denominated by different writers, the disease assumes the second stage, or becomes, as Strambio calls it, "confirmed pellagra."

This stage in the course shows a deepening of the previous symptoms in nearly every particular, and, unless checked, generally progresses to a fatal termination.

The following quotation from Casenave, written over fifty years ago, may be fitly used in this connection, as showing the difficulty in making any definite classification of the course of pellagra:

"The division of pellagra into commencing, confirmed, and inveterate is not a practical one, for pellagra may be beyond hope from its commencement. The expressions *period* and *degree*, which convey the idea of certain fixed symptoms and appearances, are not adapted to the description of a disease so capricious. The term *degree* seems

to indicate an increasing intensity, while the second or third appearance of the disease may be less severe than at first. When we employ these terms, therefore, we shall use them only as symptoms of a more or less advanced step of the disease, for, like every other disease, pellagra has a beginning, a progress, and a termination."

An added difficulty in following the course of pellagra lies in the absence of well-marked lines of demarcation between the different so-called stages. The intermittent may imperceptibly merge into the confirmed, or even the apparently confirmed may seem to improve into the remittent or even the intermittent form.

When a patient reaches this stage, however, the pellagra seldom remains stationary; it either decidedly improves or the reverse. The condition has become so intolerable that efforts are made for relief, so that either amelioration of the trouble ensues, or the general system shows an inability to cope with the poison. In this stage, also, the mental abnormalities either deepen or clear up, and the various psychoses are liable to become confirmed.

Should the progress be unfavorable, a general cachexia may set in, sapping practically every organ in the body. By active treatment this cachexia may be halted or even driven back, but when pellagra has advanced to the deeply cachectic state, with weakened mentality, it may safely be assumed that trophoneuroses have taken place, in which degenerations and scar tissue lie behind the open manifestations.

There is the utmost difference between the progress of pellagra in robust individuals, with healthy ancestry, good habits, hygienic environment, financial ability to



• Unusual pigmentation in pellagra. Patient died ten days later. (Courtesy of Dr. J. W. Babcock.)

provide nutritious food, and intelligence to so regulate the mode of life that the diseased body can wage a strenuous fight with the toxins that seek to destroy it. These are the cases who enable the physician to furnish optimistic reports concerning pellagra, and, were it not for such as these, the usual progress of pellagra would be most discouraging.

The ravages of this malady in some of the congested and poverty-stricken localities of Europe have caused many to consider it a disease of poverty. This is an error. It is a disease of all classes, but its progress among the physical or mental weaklings, among those who cannot stop long enough in the battle for bread to deliberately and systematically fight this monster—these are the stricken ones, who yield to its every inroad and who permit its rapid advance.

We may sum up the progress of pellagra by the statement that in many instances its course is most erratic, but that in normal individuals it is an extremely chronic disease, and that a duration of from five to fifteen or even twenty-five years is not uncommon.

PROGNOSIS

It may be emphasized at the outset that pellagra in any degree, however seemingly slight, is a serious disease. The simplest manifestation is a proof that there lurks in the system a subtle, a mysterious, an intangible toxin, one whose lair has not as yet been located, or whose intimate composition been understood. We are, therefore, in a sense, fighting an unseen enemy, and until this enemy is forced into the open, we must necessarily rest in an uncertainty.

Our experience with pellagra in the United States has been too limited to form reliable conclusions as to its mortality, most of our few statistics being based on asylum records. It is natural to suppose that such statistics would be very high, for none but the advanced cases are sent to asylums—cases where trophic lesions have done their destructive work, or where cachexias have sapped the scant vitality of the invalid.

Asylum statistics to date give the startling mortality of 67 per cent., though this is not based on a very large number of cases.

Statistics on non-asylum cases in the United States have not been collated in sufficient numbers to furnish any definite or reliable information, but the writer feels that there is much reason for optimism as to the future outlook of the situation, and little excuse for the attitude of wooden pessimism assumed by some, who are supposed to be in a position to speak with authority.

Lombroso, as quoted by Dr. Lavinder, stated that in 1883 there were treated in 866 Italian civil hospitals 6025 pellagrins, of whom 923 died; in 1884 there were treated in 993 hospitals 6944, of whom 780 died, thus giving, in this large experience, an average case mortality of nearly 13 per cent.

Wollenberg (Public Health Reports, July, 1909) estimates from reports he considers fairly reliable a total of 55,029 cases in Italy in 1905, with a total mortality of 2359, a mortality of a little over 4 per cent. Allowing for possible errors, this does not seem such a very gloomy report.

Early cases, those recognized before cachexia has set in, cases in the intermittent stage, where periods of seeming

health intervene between the pellagrous manifestations; cases where little involvement of the nerve-centers is apparent; cases which possess enough intelligence and perseverance to continue treatment for a long time; cases with strong ancestry, without syphilitic or other hereditary taint—these individuals may rightly cherish strong hopes for ultimate and complete recovery.

Other factors of important prognostic import relate to habit and environment. Those who are not willing to regulate their daily habits strictly along hygienic rules as laid down by the medical attendant may expect unsatisfactory progress, frequent relapses, and probably an unfavorable termination. Probably the most dangerous indulgence is that of strong drink. Alcoholic beverages, unless in the smallest and most attenuated form, are poisonous to pellagra, and it is wise to inform the patient of this fact without any quibbles. The writer would not feel justified in giving any "steady drinker" a hopeful prognosis, no matter how early in the disease the true condition is recognized.

Again, if the pellagrin can spend the heated term in a cool locality, the outlook is greatly brightened. Unfortunately this is impossible in many instances.

Speaking generally, it might be said that the earlier the disease is diagnosed and treatment begun, the more favorable the prognosis.

The amount of skin involvement is not a fair criterion of the gravity of the invasion, though a clearing up of these lesions is to quite an extent an index of improvement.

The chronic types, where there have been several recru-

descences, but neither cachexia nor mental involvement, may be considered as hopeful.

Pellagra being ordinarily an afebrile disease, the presence of fever, particularly if decided or persistent, may be looked on with grave apprehension.

The nervous, and especially the psychic symptoms furnish more reliable indices as to underlying trophic changes or degenerations. Therefore, where marked mental symptoms supervene, where a melancholy or a settled gloom pervades the temperament, or, worse still, if dementia with loss of reflexes complicates the situation, the outlook is correspondingly darkened.

The writer always gives a guarded prognosis in cases with mental involvement, and advises his readers to do likewise.

Another form in which death may be confidently predicted is the so-called typhoid pellagra. When, in the course of the pellagra, there appears opisthotonus, rigidity of the legs, delirium, albuminous urine, with ammoniac odor of the perspiration, tremors, and fibrillary contractions, accompanied by high temperature, the end is not far off.

There are certain complications which exert a decided bearing on the ultimate result; among these are malaria, intestinal parasites, nephritis, acute bronchitis, pneumonia, bed-sores (often impossible to avoid), tuberculosis of the bowels, pregnancy, or any acute intercurrent affections.

Occasionally, after the patient seems on the road to recovery, a severe recrudescence, without apparent cause, greatly clouds the prognosis.

As in any other chronic affection, pellagra renders the

body more vulnerable to infections or epidemic diseases. The physician should always bear in mind that in pellagra we are treating a disease entity, the etiologic foundation of which is not settled, and until this "consummation devoutly to be hoped" is realized, we should in every case be exceedingly careful as to promises of recovery. In addition, remembering its seasonal character, a full year, unbroken by any pellagrous symptoms, should elapse before an opinion as to cure should be expressed. Especially is it to be desired that the patient should pass the following spring and early summer with no sign of a recrudescence.

Should this fortunate state of affairs take place, where the skin lesions have disappeared, where the digestion seems normal and the diarrhea has abated; should the drooping spirits regain their wonted vivacity, and the wasted body put on again a liberal amount of adipose tissue, and should this improvement last for a year or more, the pellagra may be considered cured, and the patient may reasonably indulge in the hope that the mysterious poison has departed never to return.

CHAPTER VIII

THE TREATMENT OF PELLAGRA—A DISCUSSION OF DIFFERENT METHODS

It is admitted at the outset that a specific treatment for pellagra has not been found.

When, in any disease, a multiplicity of remedies are laid down, it is proof positive that *one* sovereign remedy has not been discovered. This is unfortunately true to a degree in pellagra, but the accumulated experience of many students with methods, empiric and otherwise, has not been barren of results, so we feel that the therapy of this malady has been removed from the realm of mere guess-work, and that many of the symptoms we can attack with a feeling of confidence born of past successes.

In this chapter some of the views of different investigators will be discussed, but the writer will give a full account of the therapeutic procedures which (in his and the experience of those whose opinions he values) have yielded the best results.

Lombroso was the first to formulate any definite treatment, and some remarks made shortly before his death had a prophetic ring. He said, "The therapy of this disease, which was at first desperate, and could be summed up in baths barren of result, can now be undertaken more confidently and rationally, as the treatment of a chronic intoxication, analogous to alcoholism or morphinism, and

curable by antidotes, when the use of the toxic material has been suspended. These antidotes are probably to be found in arsenic and chlorid of sodium."

The teaching of Lombroso has met with deserved respect, and many of his ideas have formed the basis of the present therapy. To attempt to cover this subject without a review of the measures recommended by him would render the chapter incomplete.

He recommended a liberal diet, including a full allowance of meat; though in the well nourished he did not consider it so necessary to push the feeding. He also recommended baths and cold douches for the paretic state, the chronic skin lesions, and the neuritis manifested by burning sensations. In those, however, where a repugnance to baths was manifested he did not insist on hydrotherapy. He did not favor iron, for he seldom saw benefit arise from its use, while he often saw it exert an unfavorable influence on the gastro-intestinal symptoms. Acetate of lead he tried out, finding it of no avail except in pellagra of the aged. In typhoid pellagra he obtained no benefit from any procedures.

Finally, Lombroso thought of arsenic, and, after experimenting with it for a while, he came to the conclusion that in it he had found a most valuable remedy—not an absolute specific, but a remedy that acts somewhat as an antidote. In this particular he compared the action of arsenic to that of opium in alcoholism or mercury and the iodids in syphilis. Sodium chlorid he also used with some satisfaction, but seemed to think its best effect was in children. In using this drug (arsenic) he either administered Fowler's solution, beginning in 5-drop doses and

increasing to the physiologic limit, or arsenous acid (arsenic trioxid), dissolved in slightly alcoholized water in doses of $\frac{1}{40}$ mg. up to the point of tolerance. When the well-known physiologic effects appeared he would suspend the drug for a few days, begin with the minimal dose, and gradually work upward again.

Among the types which he thought arsenic benefited were cases with marked marasmus; cases with incipient paresis; cases badly run down as a result of sitophobia; cases with vague mania, but not systematized delirium; cases in aged people, if not too senile.

Among the class of cases which derived little benefit from arsenic were children and robust cases; cases with systematized delirium; cases with mental alienation of extreme chronicity; cases complicated by lobar pneumonia, tuberculosis, nephritis, or severe and oft-recurring vertigo.

Among the symptomatic remedies of his armamentarium were calomel, bismuth, castor oil, opium, tannin, and chlorate of potash. He also advocated strychnin and faradism, and in restless or maniacal cases he used opium, chloral, or paraldehyd as hypnotics.

While he claimed that even empirically arsenic had proved its beneficial effect, he also claimed that rationally it could be prescribed on the grounds of its tonic and "alterative" effect on the heart, skin, and nervous system, besides its antifermentative power in the alimentary tract.

His methods—hygienic, dietetic, and medicinal—have served in many ways as a beacon light, which still casts its rays on the therapeutics of the present time.

To review all the literature to date advocating countless

remedies, some of them more bizarre than reasonable, would demand a useless expenditure of the reader's time. Such will not be attempted, but some of the contemporaneous literature will be abstracted in order to show that the rank and file of the medical profession have not slept over this problem.

The first comparatively non-toxic preparation of arsenic was atoxyl, probably first used by Babes, and it seemed to give quite satisfactory results. Following atoxyl came soamin and arsacetin, all trade names for sodium arsanilate, and containing from 22 to 26 per cent. of this drug.

It would appear that the arsenic in these preparations is liberated very slowly in the system, thus obtaining the wished-for therapeutic effect minus the toxic. Atoxyl and the other trade preparations of its class were claimed to exert only about the fortieth toxic effect of arsenic trioxid, but in several instances unfavorable effects were noticed, among others degeneration of the optic nerve, resulting in blindness. Koch, who was at first a strong advocate of atoxyl, after getting several cases of blindness from its use, and feeling that small doses were valueless, gave it up.

Those who used this preparation began in doses of $\frac{1}{2}$ to 3 gr., given hypodermically every alternate day, and increased until the single dose reached as much as 10 gr.

Arsacetin, or sodium acetyl arsanilate, was much more soluble than atoxyl, would stand heating so that it could be sterilized, and was given in doses ranging from 1 to 7 gr. hypodermically.

Babes thought well of atoxyl from his experience in

Roumania, while Warnock, who used it in the asylum at Cairo, Egypt, was at first quite enthusiastic over his results. Later reports, however, were not so unanimous in its praise, and in one of his papers Warnock wrote, "It may be said that the value of atoxyl in the advanced stages of pellagra, such as are met with in this asylum, has not been demonstrated."

Among American observers, who have not been pleased with atoxyl after extensive trial, are Wood, of Wilmington, and Babcock, of Columbia.

Soamin is still being used in some quarters with satisfaction, but the writer does not believe that atoxyl or arsacetin is at present being administered to any great extent.

Among the next therapeutic procedures to attract attention was transfusion of blood, as advocated by Cole and Winthrop, of Mobile, who were the first in this country to champion it successfully.

These investigators proceeded upon the assumption that:

"Pellagra is an intoxication, the toxic principles existing in the blood of pellagrins.

"The production of pellagrous symptoms by the injection of blood from pellagrins, the definite precipitative, hemolytic, and antitoxic action of the serum, the artificial immunity produced in animals, and the immunity acquired in patients recovered from pellagra, are all suggestive of a serum treatment in the solution of the pellagra problem.

"Antonini and Marianni used pellagrous serum hypodermically with apparently good effects, so much so that Lombroso, in a manner, indorsed their efforts."

Cole and Winthrop, believing that the blood of a healed pellagrin possessed all the curative powers of the serum,

besides having a tendency to improve the anemia in severe cases, transfused quite a number, with seeming remarkable effects in some of the cases.

They report the following conclusions:

"(1) In certain severe cases of pellagra resisting all forms of medical treatment transfusion has been followed by recovery with no relapse.

"(2) The patients recovering showed marked improvement from the first; in the fatal cases there was no benefit from transfusion.

"(3) Transfusion is of undoubted value in certain severe and apparently hopeless cases, but without a thorough knowledge of the technic of transfusion, and without a careful selection of the cases and donors, it will be brought into an undeserved ill repute."

Possibly, for the reasons mentioned, this operation has fallen somewhat into disrepute, and perhaps undeservedly. It must be admitted that some apparently hopeless cases have suddenly showed marked improvement after transfusion, and the writer trusts that, with the improved technic, etc., as advocated by these gentlemen, transfusion may still hold a worthy place in the treatment of certain selected cases. This procedure must always be employed by a careful surgeon and under favorable surroundings, otherwise it will prove disastrous.

At present, few, if any, advocate transfusion, except as a dernier ressort.

Dr. A. C. Cudd, of Spartanburg, S. C., has reported three appendicostomies with irrigation of the colon for pellagra, and feels that decided improvement was obtained in two of them.

Another surgeon, whose name has escaped the writer, has advocated cecostomy and irrigation in pellagra.

These radical surgical operations, while they may aid in the elimination of toxins from the intestines, must necessarily be limited in their application, and will probably not be used to any great extent.

The idea that the colon is the most frequent habitat of "pellagrous germs," and that its thorough irrigation will aid in the systemic elimination, is not a new departure, but has been frequently mentioned by the older writers. It may be stated as a general principle, however, that any agencies assisting in cleansing a filthy colon exercises to some degree a helpful influence on pellagra.

Drainage of the gall-bladder has been advocated and performed in Atlanta quite recently, but the cases have been too few and the time too short since the operations to arrive at any definite conclusions as to their effect on the disease.

Along with many other systemic infections for which salvarsan has been employed is pellagra. It has almost become the custom in some quarters, when other remedies fail, to use salvarsan empirically, hoping that in some unexplained way benefit might ensue. Dr. E. H. Martin, of Hot Springs, Ark., strongly advocates both salvarsan and neosalvarsan, claiming the former to be 35 to 50 per cent. more curative than the latter.

The writer has seen it injected in several cases, and has reports on over eighty instances, where it was employed in practically every stage of pellagra, from the mild to the typhoid, and the consensus of opinion is that it is useless, unless syphilis enters as a complication.

No other special surgical treatment has been suggested.

We will now take up the general treatment of pellagra in its different phases: First, the treatment of the disease as an entity; second, treatment of the special symptoms, of which there are many, and of the complications, of which the same may be said.

The general treatment naturally divides itself into: (1) dietetic; (2) hygienic; (3) hydrotherapeutic; (4) medicinal; (5) climatic.

Dietetic Treatment.—Until the theory regarding the etiology of pellagra is clearly settled, and the present zeist views as to some products of spoiled corn being responsible is exploded, it would appear the part of wisdom to give our patients the benefit of the doubt by excluding from the dietary, so far as possible, all articles of food made from corn or corn products. We say "so far as possible," for, as has been previously mentioned, there are so many adulterated food products on the market in which some derivative of corn is the adulterant that we cannot always be sure that corn is really absent from our daily food or drink.

This would also apply forcibly to the dietaries of various institutions, especially those for nervous and mental invalids.

In the early manifestations of diarrhea, this symptom being in the main compensatory, a restricted diet has but little influence, though, of course, the ordinary care as to food with a large amount of irritating residue should be noted. This applies only to the early diarrhea before inflammatory changes of the intestinal mucosa have occurred.

Pellagra being both chronic and exhausting, active supportive measures are indicated from the very outset. Every patient with pellagra, no matter how light it appears,

may be considered to have entered into a long and taxing battle, and his daily caloric requirements should be guarded most zealously.

Along this line should be stressed the caution that when certain articles of food of which the pellagrin is fond are prohibited, the medical attendant should see to it that these articles are replaced by something else with an equal caloric value, or the nutrition will seriously suffer.

The writer has observed a number of patients where one article after another has been eliminated from the daily dietary without being replaced specifically, until the patient was not ingesting enough for an infant in arms.

The diet should be easily assimilable, highly nutritious, and it might be added that pellagrins seem to bear specially well the flesh proteins.

It has been the experience of the writer that all along through the course of the disease meats are well borne, and, even in those conditions where there is much active gastrointestinal irritation, they agree better than in a like amount of irritation from other causes. Tender broiled steak or roast beef, lamb, or other roast meats may be given twice daily, or, if the mouth is too sore to chew, either the scraped beef or that ground in a sausage mill may be served. This also applies to the white meats, and, if the suggested grinding of the meat is carried out, it is as little irritating as possible to the inflamed buccal membrane.

As a sample diet in Italy may be mentioned that at the Locanda Sanitaria at Bagnolo Mella. It is as follows: First meal, meat broth and coffee and milk, each on alternate days, with 150 grams of bread. Second meal, one liter of soup made of macaroni, 100 grams of vegetables,

100 grams meat stock and condiments; boiled meat, 200 grams; vegetables, 50 grams; bread, 300 grams; wine, 200 grams. Third meal, one-half liter of soup made of rice, 50 grams; vegetables, 50 grams; meat stock and condiments, 100 grams; vegetables, 50 grams; and wine, 200 grams. This diet is modified in many ways to suit individual tastes and idiosyncrasies, and reduced in quantity for children under twelve years of age.

Eggs are generally permissible, though, if there is a flatulent tendency, it is well to give only the whites. The albumen of raw eggs may be prepared in various ways, limited only by the ingenuity of the nurse, being flavored with orange, lemon, grape, or other juices, and when prepared this way seldom disagree. These egg-albumens are most valuable in the exhausted typhoid conditions, and may be administered early and often.

Sweet milk is valuable when it agrees, but, unfortunately, many pellagrins show an idiosyncrasy against it. Flatulence frequently follows its ingestion, and in many patients the stomachs furnish enough rennin to promptly coagulate the milk, but are tardy in disintegrating the curds, so there is present a sense of weight and discomfort in the epigastrium. Peptonizing the milk usually obviates this, but few pellagrins relish peptonized milk.

One highly esteemed confrère recommends for pellagra forced feeding, consisting of six raw eggs and three quarts of sweet milk daily, both being increased until at least a gallon of milk and ten or twelve raw eggs are consumed in the twenty-four hours. This would be practicable in a not very large proportion of cases.

Buttermilk is a most useful article of diet, seldom up-

setting the stomach or intestines. The artificially soured milk, or lacteal champagne, containing all the fat, is often not only well borne, but acts as an appetizer.

Where constipation is in evidence, oatmeal, tender vegetables in purée form, thoroughly baked Irish—not sweet—potatoes, or cereals with but little sugar will aid the peristalsis of the intestines.

Later on in the course of the disease, when inflammatory lesions have set up in the intestines, or a chronic gastritis complicates the situation, the diet should be suited to the condition, remembering, though, that to some extent the gastro-intestinal tract will bear more in pellagra than when similarly inflamed from other diseases.

Barley-gruel, rice-water, the lighter cereals, thick broths with scant condiments, malted milk and egg, dry meat powders, dry albuminized powders, with butter up to the patient's ability to eat—this is a general summary of the later diet.

Olive oil, in $\frac{1}{2}$ - or 1-ounce doses at intervals, will often help the abdominal cramps, while the addition of an egg to each portion of the olive oil will greatly swell the daily calories.

The following dietary is recommended by Dr. Joseph Goldberger in his last report, January 15, 1915, and coincides to a remarkable extent with that advocated by the writer as far back as 1909:

“**Milk.**—Fresh milk alone or in alternation with buttermilk should be given freely. It is probably the most valuable single food, and adults should be urged to take not less than $1\frac{1}{2}$ to 2 pints in the twenty-four hours.

“**Eggs.**—Fresh eggs should be allowed freely. In addi-

tion to the milk and meat, an adult should take not less than four eggs a day. In certain of the severer forms it may be necessary to give the eggs in the form of albumen-water, preferably with orange or lemon juice.

“Meat.”—The meat should be fresh lean meat. Whether all fresh meats are equally valuable in treatment we do not know; future studies will have to determine this. Our experience has been with beef alone. This may be served as scraped beef, as a roast, or as steak. Where mastication is painful, meat juice may be given instead. An adult should be urged to take at least a half pound of lean meat a day in addition to the milk, eggs, and legumes. It may be necessary in some instances to work up gradually to the point where these quantities can be taken.

“Legumes.”—We have been much impressed with the favorable results following the use of beans and peas alone. The beans and peas should be fresh or dried, not canned. The palatable pea or bean soup should be prepared and should be given freely. In addition to or in alternation with the soup the beans or peas should be served and eaten in any one of the other well-known forms.

“In cases presenting marked gastro-intestinal symptoms, the diet of the patient may be limited to the foregoing articles. It may here be emphasized that diarrhea is no contraindication to the full feeding.

“In cases presenting only moderate or no gastro-intestinal symptoms there may be added, in restricted amounts, oatmeal, rice, and barley as cereals, potatoes and onions as fresh vegetables, fresh or dried (not canned) fruits, and wheat or rye bread or biscuits.

“As long as symptoms of pellagra are perceptible we pre-

fer to exclude all corn products; not that corn is not a wholesome and nutritious food, but because the occurrence of pellagra is commonly, though by no means exclusively, associated with the consumption of a diet in which corn forms a disproportionately large part. Similarly, a reduction in the amount of other carbohydraceous articles, such as the newer cereal breakfast foods, molasses, jams, or starch, should, we think, be ordered, if on analysis of the patient's prepellagrinous dietary some such articles or combination of articles appear to have formed a very conspicuous proportion of the diet.

"After all symptoms of pellagra have disappeared, corn and other starchy foods in moderation and guarded with an abundance of milk, meat, or legumes, and, preferably, with all of these, may unhesitatingly be allowed."

The experience of the writer has rendered him chary in the use of alcohol in pellagra. It would appear that the possible fuel and food value of alcohol is more than counterbalanced by its malign effect on the gastro-intestinal mucosa, as has been noted in a number of instances where this agent was added to the dietary in apparently convalescing cases. In exceptional cases, when whisky or brandy are deemed necessary by the physician, they should be well diluted, and be given as milk-punch, egg-nog, or with grape-juice or lemonade.

Practically the same may be said concerning the alcoholic proprietary food preparations. As an aid to the daily regimen or to tide over some dietetic emergencies some of them are useful.

During intercurrent attacks of vomiting, when no food can be retained, or where more solid nourishment is omitted

during the night, calling for some slight stimulant, they fill an indication, but as a dependence to supply daily caloric requirements they are a "delusion and a snare." To furnish sufficient calories with these preparations alone would keep the patient in a state of alcoholic coma plus all the resultant evils reflected on the whole alimentary tract. This is no imaginary picture, but has been impressed on the writer by observation of some melancholy instances, where zeal had outstripped discretion, and where evidences of alcoholic intoxication were thoughtlessly attributed to other causes.

To wisely adjust the daily regimen to each individual case, respecting idiosyncrasies, likes and dislikes is no easy task, and will require both time and patience. The problem of the bodily up-keep in pellagra is of basic importance, and should never be lost sight of from the beginning of the management. Its successful solution will in most instances decide the ultimate prognosis, marking the difference between recovery and death.

Hygienic Treatment.—In no other chronic or exhaustive disease is there a greater necessity for hygienic habits than pellagra. At best the patient has an up-hill fight, and both body and mind need every aid that can be afforded.

One of the first hygienic considerations is rest. As far as practicable this should be enforced, while any evidences of bodily weakness, nervous irritation, or mental instability are evident. The patient should be put to bed for a while, and every disquieting factor removed. Good ventilation, not too much light, freedom from disturbing noises, cheerful companionship, and all that train of helpful influences that prevent confinement being so irksome

are indicated. In those cases where it is not possible to obtain complete rest, active exertion should be avoided, and the judgment and tact of the attending physician invoked so as to meet the exigencies of the situation.

In the neurasthenic or mentally disturbed class of pellagrins, complete rest is absolutely essential, and no marked or lasting benefit may be expected without it.

In this division of treatment may with propriety be mentioned the avoidance of light—sunlight in particular.

The rays of the sun, especially in the spring time, seem to exert a peculiarly irritating effect on the erythema. The patient should be cautioned to keep out of bright sunlight as much as possible, and, when out-of-doors, to protect the hands and forearms with gloves, and the face and neck with a broad hat, veil, or umbrella.

It has been observed many times that an improving erythema, or even a comparatively normal skin surface, will quickly flare up on injudicious exposure to the rays of the sun.

The use of the Röntgen ray, either for diagnosis of any condition or therapeutically, should be absolutely interdicted during the course of pellagra, and for at least one year after all symptoms have disappeared. Even a brief fluoroscopic examination is dangerous.

The writer has reported two cases (*American Journal of Röntgenology*, November, 1914) in which, after exposure to the rays, violent pellagra promptly developed. In neither of these patients was pellagra suspected previous to the Röntgen examination.

As there is good reason to believe that latent or atypical pellagra may be fiercely precipitated by the Röntgen ray, its employment should be avoided in all suspicious cases.

The patient should be enjoined to thoroughly masticate the food, so as to put no undue burden on the gastro-intestinal mucosa. Parenthetically, in this connection, might be noted the advisability of putting the teeth in order. A regular examination of the oral cavity will reveal many foul conditions, where tender or defective teeth or pyorrhea alveolaris not only render effective chewing impossible, but a constant supply of pathogenic bacteria from this cavity augments the auto-intoxication already present.

The specific cause of pyorrhea alveolaris and dentalis has apparently been placed upon endamebæ by M. F. Barrett and Allen J. Smith.

The writer recommends that in all pellagrins with the slightest indication of buccal infection, a $\frac{1}{2}$ -grain injection of emetin be given every day for six days. After two weeks have elapsed this should be repeated; and, if the mouth remains sore or unclean in appearance, the "six-day treatment" with emetin may be repeated four or five times.

It is well, also, in addition to any other methods of treating the sore mouth, to have the patient wash his mouth twice daily with a solution of 3 drops of fluidextract of ipecac in a half-glass of water. This does not eliminate the necessity for appropriate dental attention.

The importance of obtaining a hygienic state of the mouth, the main portal of entry to the body, has been underestimated, and the medical attendant will find the time and trouble expended in putting this cavity in order well spent.

Sleeping in the open air, as in tuberculosis, has been advocated by some, and has its advantages when properly

followed. An abundance of fresh air is in order at any stage of the disease.

Regular hours for sleep, for rest or recreation, or for any occupation, no matter how light, must be scrupulously kept; for the slightest form of dissipation will react injuriously on the sensitive alimentary tract and unstrung nerves.

As in the dietetic regimen, each individual case will have to be managed on its merits, regulating the habits in accordance with the financial ability, temperamental status, or varying phases of the illness.

Hydrotherapeutic Treatment.—The effects of hydrotherapy in pellagra have in many instances been so beneficial that, whenever practicable, some forms should be invoked.

Hot or cold baths, simple and medicated, douching, packs, moist or dry rubs, accompanied by special massage, have proved their worth, bringing about increased oxidation of the tissues, more rapid elimination, greater metabolic activity, sharpened appetite, improved digestion and assimilation, and a noticeable tonic effect on the whole living organism.

Among the indications for well-directed hydrotherapy are vertigo, stuporous states, parasthesias, tremors, rigidity of the limbs, insomnia, constipation (occasionally diarrhea), and other neurasthenic manifestations, numerous as they generally are.

Either hot or cold baths may be employed, the hot being more grateful to the extremes of life or the feeble. It has been ascertained that practically the same tissue changes follow a hot bath as a cold one, being caused by an effect on

the innervation or the muscles; in fact, all combustion processes in the body are referable to the muscles. A simple hot-air bath may have little effect, but a series of hot-air or hot-water baths increase nitrogen elimination, urea elimination keeping pace with the excretion of nitrogen, and uric acid is also excreted in greater quantity.

"Elaborate studies of these metabolic changes have been made by many observers, and in connection with ordinary hydriatic procedures, the half-bath, the Scotch douches, etc. It is interesting to note that Hippocrates states that the temperature elevation which occurs in connection with most acute infectious diseases is, within limits, remedial in purpose and effect. It apparently follows that temperature elevation baths may be beneficial in aiding resistance to infection, especially when followed by a short cold bath, by favoring the production of alexins and antitoxins. It seems to us, however, that cold baths are better, practically, in the infectious fevers—witness the brilliant results attained by the Brand treatment of typhoid fever. That baths of such obviously different character lead to very nearly the same physiologic results is one of the seeming paradoxes of hydrotherapy. This is recognized in practice, for, if patients do not react well to the cold baths, it is well to give a bath at 110° or 112° F.

"Dr. Simon Baruch explains this seeming paradox by the physiologic fact that both heat and cold are thermic irritants, which, briefly applied, excite the peripheral sensory terminals and thus stimulate. The secondary effects differ decidedly if the application be prolonged" (Hinsdale).

A few specific directions for some of the baths will be given, taken in the main from Dr. Hinsdale's excellent work on hydrotherapy.

The Warm Full Bath.—A large tub is filled three-quarters full of water at 95° to 100° F., in which the patient is fully immersed, first having his head covered with a wet cloth in cold water. The room should be at a temperature of about 80° F., and means should be at hand for maintaining the water at its initial degree of heat, for this bath is usually prolonged to ten, fifteen, or twenty minutes or more, as required. Indeed, the duration of a bath has been extended by Hebra and others to days and even months, the patients, some of whom suffered from extensive burns, bed-sores, pemphigus, and other skin diseases, existing in the continuous bath for remarkably long periods. If continued for several hours, the patient may sleep in the bath, but he naturally requires constant attendance, special lifting apparatus, and electric and other appliances for maintaining a constant temperature. For dermatologic purposes 100° F. is considered best. Mutton suet, lanolin, or petroleum applied thoroughly to the skin protects it from puckering or peeling.

Hot baths of greater or less duration, as described above, can exert a most helpful effect in some of the neurasthenic pellagrous patients where all other methods have seemed unavailing, and the physician is importuned to redouble his efforts, in the slender hope that some good may arise.

The Cold Bath.—For fairly vigorous persons the best time for the cold bath is before breakfast. Weak or delicate persons may take it in the forenoon. Chill, languor, or drowsiness coming on after cold baths are contraindications

to their continuance; tepid baths are then to be substituted. Vigorous friction should always follow the use of cold.

The water of a cold bath is usually drawn in a tub from the public supply, and varies, according to the season, from 40° to 70° F. The cold bath is the favorite of the Anglo-Saxon race and in those who need to get up a reaction; for the drowsy pellagrins of the "florid type" or for the robust who tend to a high temperature the plain cold bath is often most grateful.

Salt Bath or Rub.—This may be given as follows: The patient is placed in a tub of warm water, the temperature of which may be practically judged by the hand, which should be able to bear it with comfort. The salt should be of a fine quality and should not contain coarse particles. A good kitchen or cooking salt answers all requirements. The attendant, having stood the patient up in the tub, wets his hands and dips up a handful of the salt. With it he thoroughly and firmly, but not roughly, rubs the body all over for some fifteen or twenty minutes. The patient is then made to lie down in the water, the salt is washed off, and after a few minutes a cold douche is given. He is then put to bed at rest for a time. This may be done three or more times weekly.

Where a powerful effect on the nervous system is desired the Scotch douche, which is an alternating douche of hot and cold water or steam and cold water, may be used. The facilities for these special forms of hydrotherapy are found only in properly fitted institutions, and their application should be entrusted only to those who are trained to scientifically use them, or harm might result.

The use of *rectal douches* for proctitis, tenesmus, or over-

loaded rectum, or irrigation with the recurrent rectal tube (Kemp's) for sedative or cleansing purposes, have their useful place, and do not vary materially in their indications or application in similar bowel inflammations from other causes than pellagra.

The same may be said of vaginal douches.

At all times the patient should be urged to drink a sufficiency of water, so that the blood-pressure may be maintained, the fecal current well supplied with moisture, the kidneys freely flushed, and, by the solvent power of the water, the eliminative functions be enabled to dispose of a maximum of toxins.

The question of *gastric lavage* in pellagra is a somewhat complicated one. As a routine measure it holds no place. The gastric disturbance is not primary with the stomach any more than it is with the skin, and to attempt to control the digestive manifestations by lavage would necessarily prove disappointing.

Where catarrhal gastritis complicates the trouble, or a deficient motor function of the stomach or a stenosis of the pylorus permits an undue damming of the stomach-contents, lavage at not too frequent intervals will afford some relief.

When this procedure is employed, it is well to use first plain warm water, then the medicated fluid, then follow up with plain water.

Should the lavage be followed by colicky pains or should the tube irritate the fauces, it is wiser to either discontinue it or use it at infrequent intervals.

Medicinal Treatment.—The application of medicinal remedies in pellagra is, in the opinion of the writer, fruitful of much benefit. Many of the most distressing symp-

toms can be either relieved or mitigated, and just because a positive specific has not been found is no reason why a therapeutic pessimism should be allowed to dampen the ardor of the physician. Therapeutic pessimism is the inevitable refuge of the weakling, and if the medical attendant is imbued with that spirit he should hesitate in treating pellagra.

For the sore mouth and tongue an application of nitrate of silver (20 grains to the ounce of water) daily or on alternate days is recommended. A mouth-wash of boro-glycerin (25 per cent.), or half-strength liquor alkalinus antisepticus, or a combination of chlorate of potash and glycerin, with rose-water as a vehicle, will generally prove satisfactory. For the aphthous ulcers, oftentimes so painful, gentle "touching" with half-strength aromatic sulphuric acid once daily, or a liberal application of a mild solution of salicylic acid in glycerin and alcohol, will be sufficient.

The emetin treatment, as previously described, will in many instances promptly abate the sore mouth.

For the salivation give $\frac{1}{200}$ grain atropin every four hours till the dribbling ceases; then stop, for the continuance of the atropin would cause uncomfortable dryness of the mouth and fauces.

Should the interior of the buccal cavity and fauces become dry and uncomfortable, a frequent spraying with liquid albolene, to which a little menthol has been added, will prove most grateful.

As a constitutional treatment the writer recommends the following, which has been evolved from his own experience, augmented by suggestions from others in whom he has confidence.

At present the writer employs for hypodermic use 16-minim ampoules of iron arsenite solution, and ampoules of sodium cacodylate, 1 c.c., each ampoule containing $\frac{3}{4}$ grain of the drug. One of each is injected on alternate days, injecting them under careful aseptic precautions. This injection on each day, but alternating the drug, is kept up for two or three weeks, then the injection is given every second day, still alternating the ampoules, for two or three weeks longer. After that the injections are given only about once a week (still alternating), as long as it is practicable or considered advisable.

Internally it is recommended that a combination of Fowler's solution and a saturated solution of potassium iodid be given, beginning in 5-drop doses and increasing 1 drop daily until the physiologic limit is reached. Generally the puffiness under the eyes appears when about 25 to 30 drops are being taken. When this appears, the drops should be discontinued for two days, and started at the minimal dose of 5 drops, increasing gradually as before. Some can take larger doses without discomfort than others, but it answers no good purpose to push it after the physiologic limit has been reached. Occasionally the patient, on account of excessive irritability of the alimentary tract, will prove intolerant of arsenic internally. Should this be apparent, the saturated solution of potassium iodid alone may be pushed, given in a little sweet milk.

This is the formula:

R. Liquor potassii arsenitis.....	3 drams.
Saturated solution kalium iodid.....	5 "

The number of patients who could not tolerate this formula have been extremely few.

After the active symptoms of pellagra have abated, and iron does not seem to be indicated, this formula may be kept up almost indefinitely in 6- or 8-drop doses three times daily.

For the frequent diarrhea, bismuth-betanaphthol and resorcin, given with milk of bismuth as a vehicle, has generally been sufficient. This failing, there may be given tannigen, protan, or heavy doses of bismuth subgallate. As a last resort, powdered opium or tincture of opium may be used, but opium, as an intestinal astringent in pellagra, has its disadvantages, as it seriously interferes with the much-needed elimination. The writer prefers 10-grain doses of tannigen, given as indicated by the severity of the diarrhea.

When there is a paucity or absence of free hydrochloric acid in the gastric secretions, 10 or 12 drops (not more) of dilute hydrochloric acid, well diluted and given thirty minutes after meals, will often greatly aid digestion and lessen the "heavy feeling" so much complained of.

For the anorexia, tincture of nux vomica, condurango, calumba or quassia, with compound tincture of gentian or cinchona as a vehicle, will often sharpen an indifferent appetite if given a short time before meal time.

In anemic or cachectic conditions the various ferruginous preparations are indicated, as well as cod-liver oil, olive oil, or official preparations of the hypophosphites.

A malarial complication, often present, either openly or latently, will require the addition of quinin, which may be administered in the most eligible form.

Constipation, when present, may be controlled by castor oil or enemas, drastic cathartics being inadmissible. In

these infrequent cases of constipation in pellagra an injection of 2 to 4 ounces of cotton-seed or olive oil, introduced into the rectum on retiring and kept in all night, will generally produce a soft, unirritating and effectual evacuation of the bowels the next morning.

The writer is also employing, with good results, the liquid paraffin, given as required—generally a tablespoonful night and morning.

Mention might also be made of phenolphthalein, which, in 1- or 2-grain doses at night, is followed by satisfactory movements.

At present, reports of the use of hexamethylenamin are being sent in with some frequency, and it may be found that in this preparation a useful agent has been found. Its physiologic elimination in the urine, bile, cerebrospinal fluid, and other fluids of the body may enable this drug to exercise an antitoxic effect.

Ichthyol, too, is recommended by some.

The symptoms of nervous irritation, expressed by burning hands, feet, or mouth, will often tax to the uttermost the resources of the physician. These may be combated by compresses saturated with a mild solution of bichlorid of mercury, ice cold, and applied at frequent intervals; by baths in hot mustard water or very slightly mentholated applications of liquid albolene. In occasional instances this burning becomes so intolerable as to require an anodyne.

The aches and shooting pains may often be alleviated by 5-grain doses of acetylsalicylic acid, given four times daily. This sometimes burns the stomach, but not often. Phenacetin, to which is added a small amount of citrate of

caffein, may also be employed for the headache or the different neuralgias.

Massage in some instances affords decided relief in muscular pains, and the rubbing in of a gently stimulating liniment is not amiss.

The erythema, being a secondary symptom, should receive only palliative treatment. Too many applications tend to irritate more than soothe, and too many ointments can sometimes transform a dry erythema into a moist one, which is far from being desirable.

While the hands are red and hot, a lotion, as suggested by Dr. Babcock, is serviceable:

Pulv. calamine.....	4	drams.
Pulv. zinc oxid.....	3	"
Rose-water.....	2	ounces.
Lime-water, to make.....	1	pint.

This may be applied *ad libitum*.

After desquamation begins, there are several mild ointments available.

The writer has used with satisfaction the 5 per cent. boric acid ointment. Dr. Babcock recommends:

Pulv. calamine.....	$\frac{1}{2}$	dram.
Zinc oxid.....	$\frac{1}{2}$	"
Olive oil.....	1	"
Lanolin, to make.....		1 ounce.

Gentle cleansing of the scales or crusts, after having been softened with some oily substance, will promote the comfort of the patient.

When other applications to sore and crusted skin have failed, the writer recommends the scarlet-red ointment (Heilkraft). This may be applied once or twice daily and is quite efficacious. An objection to its use is the stain it produces upon any article it touches.

When the erythema attacks the eyelids and sympathetic conjunctivitis ensues, a weak solution of argyrol dropped in the eyes will generally prove adequate for relief.

For great exhaustion, the intravenous injection of saline solution (300 c.c.), every day or alternate day, is suggested.

For the mental and psychic symptoms, appearing as they do in such multitudinous forms, only general suggestions can be made. To treat these manifestations by any rule-of-thumb would be irrational and fruitless.

Sleeplessness may be combated by chloral, trional, or veronal. By the addition of phenacetin to veronal the good effect is augmented and disagreeable after-effects prevented. Morphin or codein for insomnia is to be deprecated.

Tincture of opium or powdered opium are useful for the melancholia, but they must be aided by isolation and rest.

Dr. Hansell Crenshaw believes that the degenerative changes in the cord and brain are best resisted by iodids, mercurials, and arsenic. In short, he believes that the ravages of pellagra upon the nervous tissues are similar to the ravages of syphilis upon these tissues, and that the treatment should be parallel. His explanation of the apparent failure of salvarsan to aid pellagra is based on the hypothesis that the drug has not been adjusted to pellagra by 606 careful experiments, as it has in syphilis.

When the mental symptoms deepen into the more pronounced forms of melancholia or lapse into dementia or amentia, the patient should be put in an institution for the mentally sick. These unfortunate invalids are subject to so many varying moods, suicidal and otherwise, that it is almost impracticable to properly and safely care for them at home.

While many of the pellagrous neuroses and psychoses are the result of degenerative changes, where scar tissue impedes and cuts off conduction, still, in many instances, if the treatment is persisted in with a spirit of optimism, unexpected improvement may brighten a gloomy prognosis and light may emerge from sad obscurity.

We are not as yet thoroughly conversant with the influences of the mind over metabolic processes upward or downward, and, while due caution should always be observed in any predictions, *no one man nor set of men are privileged to abrogate the functions of a supreme court by asserting that pellagra is an incurable disease, and that medical treatment is valueless.*

Climatic.—Pellagra, being in the main a disease of hot weather, it has been found in nearly every instance that a sojourn to a cooler climate was beneficial. Cold climates, or those where the winters are long and the summers correspondingly short, have never seemed to furnish a congenial soil for the spread of pellagra.

Goldberger believes that a change in climate is valuable only in proportion to the degree and character of the change of diet it involves. With this assumption the writer does not agree.

Pellagrins, unless too far advanced, get better with cold weather, and only the practically hopeless cases go on to exhaustion and death in the winter season.

Many, from financial or other reasons, cannot seek a cool climate, but all that can should avail themselves of this aid. In this country, in order to reach a cool climate in the summer time, a high altitude must be sought, and careful advice must be given regarding the influence of altitude on the vital organs.

It has been the experience of the writer and others that the benefit to the pellagrous symptoms nearly always exceeds the possible danger of high altitude, and, unless there are strong reasons, this consideration should not prevent climatic change.

In order to reap the full benefits from this change the writer believes that the pellagrin should avoid hot weather for ten or twelve months after all symptoms have disappeared.

Where it is not practicable to reach an actually cool climate, a lesser change is sometimes beneficial, but the change should always be to a higher latitude and altitude —never a lower one.

This, in both a general and specific manner, covers the treatment of pellagra. Much of it has, of necessity, been rather general, but the writer feels that the therapeutic field, according to the present knowledge of the disease, has been fairly covered.

Our pellagrous charges expect an honest effort to be expended in their behalf; they demand it, and we, as healers of the sick, have no right to consign them to the "slough of despond," nor have we the moral claim to banish this disease to the limbo of "incurable affections."

Let us, therefore, give our suffering and disconsolate pellagrins the full benefit of our knowledge as we acquire it, hoping in the meanwhile that the discovery of a specific treatment may be attained in the near future.

CHAPTER IX

THE PROPHYLAXIS OF PELLAGRA

THIS important chapter in the discussion of pellagra unfortunately must be approached from a theoretic standpoint, for, until we have positive information as to etiology, we are necessarily dealing in assumptions, not in proved facts.

One of the first questions that arises is concerning the communicability of pellagra, for on that hinges much of the prophylaxis.

The consensus of opinion at present is against the possibility of this disease being either contagious or infectious, but toxicochemical, and, as such, it cannot be transmitted from one individual to another.

As early as the middle of the last century Roussel wrote: "It can be said of the contagion of pellagra that it is a question fully determined—pellagra is not contagious."

To admit this, or to attribute the spread of pellagra to a contagion or an infection, would bring up the questions of isolation and quarantine, serious questions to individuals and communities, unless supported by strong reasons.

Italy has suffered and so have other European countries, some of whom have apparently solved the problem, but it was solved according to the zeist doctrines.

Apart from the ordinary precautions, hygienic and dietetic, already considered, the prophylaxis will be covered by an account of the methods of prevention in other countries,

that, from their long and trying experiences, we may learn and perhaps utilize some of their methods.

Joseph II., of Austria, was the first sovereign to concern himself with pellagra, giving those who sought to prevent and treat it all the aid in his power.

The first serious attempt in Italy to deal with the problem was in 1879, ten years after Lombroso's fame was established.

Much of the following is extracted from the consular report rendered by the late Bayard Cutting, Jr., and published by the United States Government.

In the year above mentioned a census was taken of the pellagrous patients in Italy, and as a result of the census a bill was introduced for the regulation of corn cultivation and importation, and the establishment of desiccating machines. The bill failed, and the only immediate result of the census was an annual grant of 36,000 *lire* from the Government toward the relief of pellagra—about 6 cents for each patient. This amount was raised at a later date, until it amounted to 70,000 *lire* in 1889; and under the law of 1902, 100,000 *lire* are contributed annually for the prevention and cure of pellagra, and as much more for the introduction of improved methods of agriculture. The census of 1879 was an epoch-making event. It brought home to the people, as a whole, the gravity of the situation, and it stimulated the various provincial governments to act independently. Many provinces appointed pellagrologic commissions, took censuses, and founded hospitals or "local sanitariums." From 1879 to 1903 was a period of local and provincial activity. The conclusions of doctors were tested on a small scale, and the way prepared for gen-

eral legislation. Meanwhile, in 1895, the Crispi administration issued an ordinance forbidding the importation of spoiled corn, and providing for inspection at chief ports. In 1902 the "law for the prevention and cure of pellagra" was passed, and in the following year was issued the regulations for the enforcement of the law. Since that time five years have elapsed, and already pellagra may be said to be a doomed disease. The statistics, so hard to interpret as regards particular details, bear unmistakable testimony to a general decline in the disease under the operation of the law.

The main provisions of the law and regulations are as follows:

I. Absolute prohibition of the importation, sale, holding for sale, or grinding of spoiled corn or products of corn destined for human food. If the corn is destined to feed animals or to be used for other purposes, it is admitted only by special permit of the prefect.

II. Obligation upon all communes to report cases of pellagra. A commune with several cases is declared pellagrous, and falls under the following provisions:

(1) Government inspection of all corn dried, stored, and consumed in the commune.

(2) Obligation on the part of commune and province to establish public desiccating plants, to provide curative nourishment for all patients, to provide patients and their families with free salt, and to treat severe cases in special institutions.

III. Establishment of pellagrologic commissions in all provinces affected with the disease.

IV. Assignment of a government grant of 200,000 *lire*

annually, and obligation upon the provinces and communes to defray, in equal portions, the expenses entailed by the act.

This is the charter under which the struggle against pellagra is now being carried on. It is proposed to examine the several dispositions of the act, then to give some details in regard to certain provinces which Mr. Cutting was able to investigate in person, and, finally, to append such other data as will be of the most profit to those interested in the fight being waged by Italy against this scourge.

It will not be necessary or appropriate to enter into the public curative measures, but the well-ordered prophylactic measures will be described. Those chiefly to be noted are: The testing of corn and flour brought in at the frontier, or offered for sale or brought to the mill, the exchange of bad corn for good, desiccating plants, cheap co-operative kitchens, the improvement of agricultural methods, and the instruction of the people as to the danger of bad corn.

The first preventive measures are to protect the peasant from imported spoiled corn. He must be taught to grow corn that will ripen, to harvest it ripe, to dry and store it properly, and to see that it does not become spoiled in milling.

Such cautions do not apply to Italy alone, but might be suitably inaugurated in the United States.

Prohibition of Spoiled Corn.—As far as regards corn imported from abroad, the provisions of the law of 1902 seem adequate in most respects. All suspicious cargoes are tested by experts, and, if the condition is not satisfactory, the corn must be sent to a distillery or else be denatured. Spoiled corn can be detected in a number of ways. Such

outward signs as mildew or the smell of mold are, of course, conclusive, but they can be removed by drying in the sun; their absence, therefore, does not prove the soundness of the corn. But the consumer should be warned against any corn that is covered with dust, that is damp to the touch, or that gives forth any smell of mold when warmed in the palm of the hand. He should be on his guard against corn of a pale color with a dull surface.

There are several chemical tests for distinguishing sound from moldy corn. The first test is the proportion of ashes. It is said that no sound corn contains more than 4 per cent. of ashes. This point is doubtful, and the test requires an accurate apparatus, and is unsuitable for general use in inspecting imported corn. The second test is that of Gosio, with perchlorid of iron. Corn-flour which has been kept in double its volume of alcohol (at 80 degrees) for several days, being frequently shaken meanwhile, and exposed to the sun or to heat, is tested, after the alcohol has been filtered and evaporated away, in a bath of perchlorid of iron solution. The reaction varies in color, from a dark green to a violet blue, according to the soundness of the corn. This test, though one of the best, is not entirely sufficient. It should be supplemented by the test of acidity, since moldy corn is always more acid than sound.

The biologic test of fruitfulness is one of the best, since spoiled corn is certain to lose much of its germinating quality. The test is easy to apply, but is, of course, ineffective for corn which has been desiccated. There is also the test of poisonous content by the actual inoculation of mice.

In theory, possibly all of these tests are required, but for practical purposes it may be said that corn which ap-

pears perfectly sound, and which does not react to the perchlorid test, is pretty sure to be harmless. In doubtful cases the germination and acidity test can be employed.

Inspection of corn at the frontiers is comparatively easy, but at the mills or in the markets, and especially in the shape of flour, it is practically impossible. The flour problem is entirely beyond the control of any government; the only hope of its solution would lie in government or municipal ownership of all mills. This proposal is eagerly supported by those interested in the pellagra question; it is certainly more practical than any plan for diminishing the corn area in Italy or for prohibiting entirely the importation of corn. Whether it is likely to be adopted is as yet uncertain. Meanwhile, and so long as milling is a private industry, the effort must be made to send only sound corn to the mill.

Every province of Italy has a commission for the encouragement of improved methods of agriculture. These "moving chairs"—or, as we might call them, farmers' institutes—are active institutions which have contributed notably to Italy's great agricultural progress during the last decade.

These farmers' institutions are now in successful operation in many states in our country, augmented in some instances by trains, educational in their scope, which go from place to place teaching the doctrine of scientific farming. "Corn shows" also are being held, where the principles of raising more and better grain are inculcated to the masses in an attractive manner.

In solving the pellagra problem they co-operate very usefully with the provincial pellagrologic commission.

The pellagrologist wishes to get rid of the *quarantino* corn; the *cattedre ambulanti* show the farmer a better crop than *quarantino*, teach him how to grow it, and prove to him by actual experiments that the new crop is more profitable than the old. The rapid disappearance of *quarantino* in Lombardy and Venetia is largely the result of intelligent missionary work by these agricultural commissions. Instead of *quarantino* the peasant is taught to plant the *mathilde*, millet, mustard, or some kind of forage. There is no doubt that all of these crops are more profitable, as a second crop, than *quarantino*.

It is no small triumph to have convinced the Italian peasant of the fact, and to have induced him to abandon a traditional crop for one with which he was not familiar. Next to the inspection of foreign corn, the diminution in the supply of *quarantino* has probably accounted more than any other factor for the encouraging decrease of pellagra during the last five years.

Desiccating Plants.—Artificial drying of Indian corn was practically unknown in Italy until within a few years. Such corn as was dried at all was merely hung in the open air, on frames, at the sides of the houses. Most of the corn was stored as soon as gathered and in any storing place that was available, without regard to ventilation or cleanliness. If Italy is the home of pellagra, while Mexico and Burgundy are entirely free from the scourge, the difference may be due simply to the fact that in Mexico and Burgundy corn is fired almost as soon as harvested. Artificial desiccation is the most important of all prophylactic measures against pellagra. It has objections, however, to encounter from the farmers. The corn loses weight, they say. This

is true, but the weight lost from decay is far greater. It will not germinate. This is true likewise if the desiccation is not properly performed; but the best desiccators leave the corn with all its natural properties unimpaired. It is expensive. Not so expensive, on the whole, as the out-door frames. The best desiccator yet contrived, that of Pietro Cattaneo, dries 110 pounds of corn with a fuel consumption of one cent. Nevertheless, in order to remove as far as possible the objection of expense, the law of 1902 provides that every family may dry, at the public desiccator free of charge, so much corn as is required for the household needs. Further use of the desiccator must be paid for, but at rates which allow nothing for profit.

Desiccators are of two types—fixed and portable. The portable type has the great advantage of saving the cost of transportation of the corn. It can be carried in sections and set up in the middle of a corn belt. It is cheap enough to be within the means of the poorer classes. The fixed type, however, is infinitely preferable. The air is kept at an even temperature and circulates equally in all parts of the machine; thus none of the corn is spoiled or deprived of any of its properties. Air heated by a furnace is forced into a chamber of seven stories. Each story is a revolving wire tray, containing about 1400 pounds of corn. The top tray is filled from above. After a certain time its contents are emptied by pressing a lever into the tray below in such a way that they are thoroughly remixed. The corn thus passes gradually to the bottom tray, whence it goes to a receptacle where it is cooled by means of a ventilator, and thence out of the machine by an inclined plane. The first tray-load of corn takes seven hours to pass through the

machine; after that 1400 pounds come out each hour. The cost of the machine is about \$540, and the power required to run it about $2\frac{1}{2}$ horse-power. Larger machines of the same kind, costing about \$1840, have a daily capacity of 88,000 pounds, and require an engine of 8 horse-power. In the Cattaneo desiccator the air is forced through the trays in both an upward and downward direction; the air which has absorbed dampness from the corn is replaced constantly by dry air; the temperature is kept low (about 104° F.), with economy of fuel and without risk of injuring the corn; and the mechanism is so simple that the machine can be handled by any laborer of ordinary intelligence.

The best of the movable desiccators is probably the Boltri, which costs about \$112, but, on account of the danger of destroying the germinating power of the corn, it is best always, if possible, to employ the more expensive machines.

Desiccation, if applied to moldy corn, will remove the moldy appearance, but in order to kill the poison germ a temperature not merely uneconomical, but actually destructive of the grain, would be required. It is, therefore, of the utmost importance to prevent the use of the public desiccator for corn which is even a little spoiled.

Public Storehouses.—Another article in the law of 1902 gives power to prefects to order the authorities of any pellagrous communes to found a municipal storehouse for the use of such inhabitants as do not possess sanitary houses; yet the insanitary conditions under which corn is stored in the houses of peasants have long been recognized as a potent producer of pellagra.

Ceresoli recently said: "The greatest injury to this food is inflicted by those who are to use it. The corn is kept al-

most always in the darkest corners of the rooms, against damp walls, surrounded by dirty clothes, exposed to all human emanations, and to all those foreign substances introduced by animals and insects. . . . Pellagra will not cease until the worst houses are destroyed, the rust cleaned, and the corn stored in a place apart."

There is no doubt that the public storehouses will come, but for the present the cost of construction and maintenance and the expense of transportation are beyond the means of the Italian communes.

Rural Bakeries.—The effort to eliminate from the diet of peasants bread made of Indian corn and to substitute wheaten bread has taken shape in the establishment of bakeries, where good wheaten bread is furnished at cost. The institution is comparatively new. In 1904 there were only 77 such bakeries, and in 1905, 89; but in 1906 the number had risen to 584, and in 1907, to 591. There is no question that corn-bread will soon cease to be a common article of food in northern Italy, and the elimination of corn-bread will mean, if nothing else, added variety in the diet of agricultural classes.

Corn Exchanges.—The idea of an exchange where moldy corn could be exchanged for good is due to Prof. Ceresoli, who carried it into execution at Bagnolo Mella. The peasants bring their corn, good or bad, and receive in exchange a lesser amount of perfect flour, deduction being made for the cost of milling and for any defects in the corn delivered. The cost of the operation, which was met at Magnolo Mella by charitable gifts, amounted to 23 cents per hundred pounds of corn. At this place the exchange was popular with the community; it meets with the approval of all stu-

dents of pellagra, and it is not very expensive in the comparison with the immense benefit conferred. Nevertheless, the scheme has not been successful. In 1904 there were four exchanges, and 439 quintals of corn exchanged; in 1905 the figures rose to seven and 1145, only to fall in 1906 to five and 674, and in 1907 to four and 292, for the exchange will never give more than five kegs at a time, and usually gives only one keg, in order that the flour may not have time to spoil at home.

The following may be considered the general conclusions of those who have made this fight as to the lessons learned and the results obtained. The list of preventive measures against pellagra is by no means exhausted, and many have been suggested which have not been adopted. In general, the object is to get at the children; to prevent pellagrous mothers from nursing their babies, or, if this cannot be prevented, to see that the mothers are well fed; to treat a child the moment he or she shows the slightest symptoms of pellagra, and to send the little patient away from the surroundings where the pellagra has been acquired. There are authorities, however, and of the highest rank, who see no remedy for pellagra short of the total elimination of corn as human food. Some would forbid its importation; others, who have noticed that pellagra increases when corn is dear, would throw open the ports of the country by the removal of the protective duty. Still others wish for the prohibition of the cultivation of certain kinds of corn, or of all corn in localities where it is not "economically profitable." So long as national habits remain what they are, so long will there be a demand for a certain amount of corn. If importation is difficult, the home crop will increase, and

vice versa. It is not by legislative restrictions, but through changes in a national taste, that corn consumption can be diminished. Education of the people to the dangers of bad corn, their awakening to the possibility and pleasantness of a varied diet—there is the remedy. Much is being done to educate the people. The industrious Permanent Committee of the Interprovincial League against Pellagra edit a magazine, the *Rivista Pellagrological Italiana*, devoted to the struggle against the disease. Popular pamphlets are distributed in great numbers; popular lectures are held everywhere; big colored lithographs, representing the healthy laborer fed on sound corn and the pellagrous laborer fed on spoiled or moldy corn, hang on the walls of public lecture halls; and the pellagrologic and agricultural commissions of the different provinces multiply instructions by both precept and example. The results vary with the various districts, but they are encouraging on the whole, and they coincide with a marked rise in general prosperity. The laborer who wants to eat something else besides corn can do so to-day as he never could before. Great numbers of the rural population are employed in factories, where they obtain a varied diet. The effect of industrial life is clearly shown in the numerous decrease of pellagrous cases between the ages of twenty and thirty; many Italians spend the summers in foreign countries as laborers; when they return in the winter, it is not only with a stock of money for the family, but also with a stock of experience. They no longer care to live on polenta only. Their wives and daughters who have stayed at home may go on with the old fare, but the men require mixed diet. It is industrialism and temporary emigration, far more than the

habit of dining occasionally at a *trattoria*, which accounts for the predominance of women over men among pellagrins of the vigorous age. If the predominance is not still more marked, it is due to a contrary tendency among those to stay at home and work in the fields. Among these classes the men suffer most; possibly because they work harder, possibly because they eat more polenta, or for both reasons. One thing, at any rate, is plain—that even without government activity and private aid pellagra would be diminishing in Italy to-day. The consumption of meat is increasing rapidly; the people are living better, the farm laborer gets higher wages, and, if he accepts a part of his wages in kind, he no longer allows the landlord to pay him in moldy corn. Thus, many causes unite to aid the fight against pellagra, and for this reason it is hard to say how much, if any, of the progress is due to legislative enactment.

If we leave statistics and listen to the opinions of experts, we shall reach the conclusion that pellagra in Italy is decreasing notably both in numbers and in intensity, but that it is extending its area. The causes of the decrease have been, in the main, the improved conditions of the laboring classes through the diversification of industries, temporary emigration, scientific agriculture, and improved wage contracts; but a part, at least, of the progress is directly attributable to direct measures of prevention and cure.

Pellagra hospitals, sanitary stations, and food distribution have lengthened the life of the pellagrins and averted the worst form of the disease. Such preventive measures as desiccating plants and rural kitchens have aided in protecting the peasantry from its scourge. But, above all,

the prohibition of spoiled corn has had an immense effect upon the public health. What is needed is an extension of the government control to mills and the milling industry. And, while all ideas of prohibiting corn, either as a crop or as an article of food, are impracticable, the effort to educate the peasantry in regard to the dangers of spoiled corn, and to show him substitutes for the more perilous varieties, as well as for the unwholesome corn loaves, are not vain. In education, even more than in government control, lies the hope of pellagra's enemies. For a country like the United States many of these measures, educational and otherwise, would be just as appropriate and as successful as in Italy. The lessons learned may be largely utilized by our own students of this problem, and both the minds and consciences of the publicists should be awakened that some of these measures be speedily inaugurated.

In this connection it may be of interest to give some recommendations elucidated by Dr. Sandwith, and put before the British Government in the interest of the pellagra situation in Egypt:

I. That the village authorities of Lower Egypt should be informed by the usual methods of the Ministry of the Interior that, although good maize is an excellent food, the habitual use of bad maize produces a disease affecting not only the skin, but also the digestive and nervous systems. The question is now of increasing importance, for corn is much more cultivated than it was a few years ago, in consequence of the increase of the population and the more bountiful supply of water. On the other hand, the wages of the *fellaheen* have nearly doubled during the last fifteen

years, and, therefore, they can now afford better food, including more meat.

II. Maize is sold at the weekly market of every town; it is stored in "shunas" in all large towns, and it is, in addition, sold as a surplus stock by the *fellaheen* from their own land to their neighbors. It seems to be impossible to control or inspect the sale of maize, but I think the local authorities should be informed that it is improper to allow obviously diseased maize to be exposed for sale. But it is not the worst maize which finds its way into the market, for the worst samples cannot command a price. The poorest peasants are the chief offenders, for at the end of each year their custom is to take, in lieu of some of their wages, a piece of land, which they cultivate for themselves with a crop of maize; the most careless of them sow diseased seed, gather the crop before it is ripe, store it in damp places before it is properly dried, and habitually eat the worst ears, which they cannot sell.

The following translation, by Babcock and Lavinder, is an example of the kind of popular pamphlets now being distributed in Italy, and some of the suggestions herein contained may be perused with profit by health officers and departments interested in the subject.

ADVICE AND RULES FOR AVOIDING PELLAGRA

Spoiled corn is a cause of pellagra, and corn readily becomes spoiled, moldy, or poisonous when harvested too early, before it is ripe, and stored in places which are damp and poorly ventilated; it may also be of poor quality when imported from some other place, and may contain a large percentage of damaged grain.

Spoiled corn may be recognized by its pale or greenish color, by the shrivelled and cracked surface of the grains, which are also covered with greenish, bluish or brownish spots, by its musty odor, and its bitterish and disgusting taste.

The damaged corn also weighs less than sound corn, and the surface of spoiled grain lacks the shining appearance of the sound article.

Keep your corn, then, in places well dried and aired. Distrust white corn, because it is more likely to spoil than other kinds. Imported corn is frequently damaged.

Keep watch over your corn while it is being ground in the mills of the country.

If you have carried good corn to the mill, see to it that you receive meal ground from that corn, and do not allow the miller to substitute meal ground from inferior grain.

If your corn is ground by a roller mill, the spoiled grains are not likely to be ground into the meal.

Instead of spending your money on wines and liquors, buy wheat bread; limit your use of polenta. If you have milk, eggs, cheese, limit the sale of these articles to others, and use at least a part of such products for your own home food.

Do not be ashamed to go to the doctor if you are a pellagrin, and have yourself entered at the local sanitarium or at the economic kitchen. Get cured in time, and so avoid the hospital or the insane asylum.

Remember that pellagrins require a curative diet. It is your right to demand it, and your duty to procure it.

The cleanliness and healthfulness of your homes are necessary conditions for preventing the molding of corn

which is kept in your houses. Never keep your corn in bed-rooms, and see to it that you have proper places for the stowing and seasoning of your grain.

Keep the corn dry.

Exert yourselves to co-operate with others for your own salvation by acquiring knowledge of and interest in the application of the law against pellagra.

As in this country pellagra has proved itself a disease of the educated and well-to-do classes, in addition to the poor and uneducated, some of the above would possibly be inapplicable; some of it, however, would apply to our people, and such portions might be used to advantage.

The writer recognizes the wholesomeness and healthfulness of sound and matured corn. When the "pedigree" of the corn is known, when it has been allowed to properly dry, and has been stored in sanitary receptacles, ground without contamination with spoiled grain, and the meal protected against dampness or mold, no more eligible food-stuff can be named, possessing as it does an abundance of sustaining food elements. When, on the other hand, it is allowed to "spoil," to generate suspicious toxins, or to become an abiding place for the various molds and bacteria, corn then becomes an enemy, one to be both avoided and fought.

Other prophylactic measures consist in the ingestion of a liberal, varied, and well-balanced dietary—one containing an abundance of the flesh proteins in fresh form, and the legumes also in a wholesome form.

The studies of the Thompson-McFadden Commission have conclusively shown the infinitely greater spread of pellagra in the absence of proper facilities for disposing of

sewage. Wherever possible, a water-carriage system should be employed, and where this is not practicable, all precautions for screening and otherwise rendering innocuous the human excreta should be practised. Pellagra certainly flourishes in unsanitary surroundings.

The writer trusts that the physicians who read this book may feel constrained to aid in the enforcement of the pure food laws, and to hold up the hands of those to whom the enforcement of these laws is their duty.

The various law-making bodies should also be memorialized to so strengthen and amend our laws that corn may be frequently inspected in its journey from the field to the table, so that it may reach the masses of our people in a harmless and wholesome condition.

The mass of the American citizens may be trusted to do right if it is only presented in a proper manner, and when the people at large wake up to a full realization of the gravity of the situation now confronting us, we may expect, as did our distant friends, that wise and beneficent laws will be put on our statute books, and enforced in every nook and corner of this broad land, that will make, in the not distant future, a fading *memory* of pellagra, an American problem that was successfully and effectually solved.

CHAPTER X

DESCRIPTIONS OF SOME RECENT EXPERIMENTS ON ANIMALS, AND DEDUCTIONS THEREFROM

THIS somewhat supplementary chapter will enter into a discussion of some recent experiments on animals, in the effort to arrive at a clearer knowledge of the etiology of pellagra. These accounts are from Public Health Reports issued by the Public Health and Marine-Hospital Service, and reflect much credit on the able and scientific members of the service.

The first is an abstract from a report by Dr. C. H. Lavinder, entitled "Pellagra and its Possible Relation to Maize According to Some Recent Views," issued February 24, 1911.

Raubitschek seems to have been the first to take up, in an experimental way, the question as to the effects of exposure to sunlight upon maize-fed animals in association with the question of a possible relation to the etiology of pellagra. His first communication was apparently of a more or less preliminary character, and quite recently he has published a much more important paper upon the subject.

It is the purpose of the present article to review briefly this paper, as well as the papers of two other authors on the same subject, and to add a few details on certain matters germane to the views expressed.

In his last paper, above mentioned, Raubitschek, in his introduction, notes the immense mass of literature which has accumulated on the etiology of pellagra, and speaks in the harshest terms of the very questionable kind of work which has been done in this field.

He also comments on the fact that only seldom have the somewhat scanty results of pathologico-anatomic results been employed in attempts to clear up its etiology, and that modern microbiologic, especially serologic, technic has never, to any extent, been so used. The work which has been done, he adds, is composed in great part of misinterpreted researches on the feeding of animals, incomplete metabolic investigations, and the piling up of statistical details.

After very briefly mentioning some of the literature, he places the theories of the etiology of pellagra in three groups: the *bacterial*, *toxic*, and *autotoxic*. These theories are then briefly reviewed in a general way, and he concludes that not one of them in its present state can be considered satisfactory.

Finally, he observes that if the real cause of pellagra is unknown, we must not insist too closely upon bringing the disease into strict causal relation with the use of maize as food, and that, if any real progress is to be made, the above theories must be tested in a satisfactory experimental way, especially upon the pellagrin, before they can be accepted as of real importance.

He then in several sections takes up his own experimental researches.

He found it possible to study only briefly the numerous micro-organisms, which have been isolated from both good and spoiled maize by various workers, and presented

as the cause of pellagra. The numerous molds which can be especially grown from spoiled corn met the same fate. Since raw corn is not directly consumed as food, but only products prepared from it, he deemed the bacteriologic investigation of prepared (cooked) food worthy of more consideration than the raw material.

Nevertheless, in a preliminary investigation, largely as a matter of orientation, he did take up in a general way the flora of raw maize, and compared his results with the literature. He thought certain isolated cultures which exhibited a tolerance to high temperatures were of a special importance in consideration of the cooking of food.

The various bacteria and molds were too numerous for detailed study, so he soon confined himself to work on food prepared from maize, especially since he found that relatively few of the micro-organisms withstood a temperature of 100° C. Such micro-organisms suggested a line of work looking to the establishment of an infection of the gastro-intestinal tract by food prepared from corn.

With this end in view, he prepared polenta and cakes from both good and bad corn. These preparations were opened under sterile precautions, and, from the inside, cultures were made on suitable media, and grown mostly under aërobic conditions. In a few cases he recovered some species of *Penicillium* and *Aspergillus*, but chiefly the *Bacterium maidis*. Usually his cultures were sterile.

Next he turned to the bacteriologic investigations of pellagrins themselves, and in this work he kept especially in mind the ideas of Ceni on aspergillary infections as a cause of pellagra.

Blood-cultures from an arm vein were made from pella-

grins in all stages of the malady, and his results were constantly and invariably negative. Bacteriologic investigations of the stools of pellagrins convinced him that the intestinal flora of pellagrous persons differed in no essential way from that of healthy individuals. At first there appeared to be an unusual occurrence of the *Bacterium maidis* in pellagrous stools, but further work showed this bacterium to be, in summer, just as frequent in the stools of healthy persons, possibly as the result of the consumption of such raw foods as salads, etc.

Finally, bacteriologic investigations of the organs of pellagrins a few hours after death gave essentially negative results.

He concluded, therefore, that there exists no basis for a parasitic etiology of pellagra.

Under the idea that pellagra is due to an almost exclusive maize diet, he thought the possible appearance of specific antibodies in the blood-serum of pellagrins a matter of much importance.

Accordingly, he prepared maize extracts, and tried, with proper technic, to obtain "precipitin" reaction in blood-sera collected from numerous pellagrins in all stages of the disease. The results were always positive. In this control work, however, with both healthy persons and animals, he obtained the same result. Hence he concluded that this reaction possesses neither diagnostic nor biologic value. He omitted detailed protocols as useless and unnecessary.

In similar manner he also made use of the complement-fixation reaction, and here again nothing characteristic could be observed. His controls displayed the same result seen with the sera of pellagrins—viz., absence of hemolysis.

Next, he tried experiments for hypersusceptibility in pellagrins and in healthy persons by means of the ophthalmo- and cutaneo-reactions with various maize extracts. All of these results were negative.

These experiments, he says, still leave room for proof how pellagrins, fed for a short time on a good mixed diet, would react to a suddenly administered maize diet.

It also remains to be shown whether pellagrins, on a long-continued maize diet, may be sensitized from the intestinal tract, and whether they would react from a new supply of maize albumin with the important symptoms of hypersensitization, such as vertigo, fever, vomiting, and diarrhea, all of which are important if pellagra has any causal relation with a maize diet.

Still it is evident that both sound persons and pellagrins bear a short exclusive maize diet without reaction.

Further experiments were made upon the phenomena of anaphylaxis in animals to determine the presence of maize antibodies. Pellagrins in all stages of the disease were bled from a vein of the arm, and these sera in various quantities (5 to 10 c.c.) were injected intraperitoneally into guinea-pigs. Twenty-four hours later intravenous injections of the same sera (up to 3 c.c.) were made into these pigs. These animals showed reactions not observably different from the controls injected with sera from normal persons.

He concludes from the work of this section that antibodies specific for maize albumins (from good or bad maize) do not occur in the serum pellagrins. If these negative results do not permit any definite conclusion, still it would appear that from them one may infer that any causal relation

between the maize diet (good or bad) and pellagra is pure speculation.

In his experiments concerning toxins he sought to determine whether maize, naturally or artificially spoiled, would produce deleterious effects upon animals if used in rational doses.

For this purpose he made use of good corn and spoiled corn obtained from pellagrous regions, ground under proper precautions, and extracted for twenty-four hours in sterile tap-water. He also made extracts from a maize porridge or broth which had been inoculated with various pure cultures, isolated either from bad maize or pellagrous stools.

The extracts he obtained were variously colored, and some possessed a fatty-acid-like odor. They were kept a long while in the ice-chest under toluol without apparently undergoing further change.

With these extracts he injected rabbits (subcutaneously, intraperitoneally, and intravenously), mice, and guinea-pigs (subcutaneously and intraperitoneally). In one series he used large doses, up to 8 c.c.; in another series daily small subcutaneous doses for one to two weeks; in another series various extracts were daily mixed with the food of the animals.

In no case were changes observed which by any means could be brought to show any causal relation between pellagra and a maize diet. Frequently the animals refused the food, and hence lost weight, but in no way did the experiments justify any idea whatever that corn contained a toxic substance which by long use may lead to pellagroid phenomena in animals.

He concluded that the negative results of these experiments are worthy of note, since it would appear from them that not one of the above-mentioned theories is supported by these results, and not one seems to bear comparison with actual facts.

In continuing this discussion, Raubitschek points out that the pellagrous erythema is usually confined to the exposed surfaces of the body, and thinks that from this it may be inferred either that there is a reduced resistance of the entire body surface, and hence exposed parts are unduly sensitive to slight noxious influences (sunlight), or that eventually, under a maize diet in the body surfaces exposed to sunlight, there is developed a noxious substance (*noxe*) which produces not only local morbid changes, but also affects the entire organism. This thought is further justified by the usual occurrence of pellagrous skin changes at that season when the field laborer is most exposed to the sun. It is possible, then, that there may be some relation between a maize diet, sunlight, and pellagra.

He directs attention to the analogy with buckwheat poisoning (*fagopyrismus*) in animals. In this connection white or spotted animals, exposed to the light, suffer, while the dark animals or white animals, kept in the dark, escape. In this condition general as well as local symptoms are noticed.

The active body in the buckwheat is soluble in organic solvents, and seems to be a lipoid, in the wide sense, and is possibly related to the vegetable lipochromes.

All these phenomena stand in near relation to the so-called photodynamy—viz., that, under the influence of certain fluorescent color stuffs, the effect of light on exposed

body surfaces in animals is to produce erythema and other skin changes, with eventual death of the animal. It would seem, then, that some such idea may be entertained for a similar relation of things in pellagra, for in corn there occurs a fluorescent color stuff, and in bad corn is also found a characteristic red material. This idea opens up a new field for investigation.

Raubitschek then describes a number of experiments on animals, testing as to maize diet and exposure to sunlight; as to the effects of the quality of the maize; the effects of increased intensity of light; the effects of change of diet after appearance of symptoms; the effects of a diet of fat-free maize, and the effect of feeding maize fat.

His figures are voluminous, and some of his data quite difficult to comprehend. He, however, arrives at certain conclusions, which will be stated. He thinks he has demonstrated the presence of a photodynamic stuff in maize, and that this material is soluble in alcohol. He brings out strongly the effect upon the animals of changing the conditions of life without any modification of diet, and discusses the symptoms displayed by the animals.

He declares that he does not attempt to bring his experimental results into a strict relation with the etiology of pellagra, nor to assume for this disease a photodynamic basis, or even to conclude that pellagra is produced by an almost exclusive diet of maize, good or bad, which displays its harmful effects first under the influence of light. The inference is apparent that his results are very suggestive, but not as yet conclusive.

He comments on certain feeding experiments of other workers, and points out that the conditions of life under

which their animals were kept may explain some of their irregular results.

He notes the effect of rice diet on his animals, and says this cereal also is rich in fat, and by many is held accountable for a disease somewhat analogous to pellagra—viz., beriberi.

In further discussing his conclusions, he says that the possibility should be borne in mind that pellagra and pellagroid affections may be due not only to the use of maize as a food, but also to the use of other grains or other plant stuffs which are eaten in various localities. Hence, observations at various places and at various times might help to explain the vexed question of a “pellagra without maize.”

This phase of the etiology of pellagra has not as yet attracted very much attention in America or English literature, but is worth considering, especially as the subject is still *sub judice*.

Lavinder comments on Raubitschek's experimental labors, but does not commit himself. As he remarks, the question of *photodynamic substances* and their effects is a large one, with a rather extensive literature. References have already been given to some of this. It may be briefly said, in a general way, that a great number of fluorescent bodies, both vegetable and animal, which are harmless in the dark, have been shown to possess highly toxic properties in the light, especially direct sunlight. These properties include the power of exerting a deleterious influence on animal body cells and on certain protozoa. In this series of substances are found normal constituents of the animal body, such as hematoporphyrin.

Fagopyrismus is an interesting condition which arises in white or white-spotted animals fed on buckwheat and exposed to the sunlight. It does not develop in dark animals nor in white animals kept away from the light. It is not due to the buckwheat, but to other species of *polygonum*, and may arise from the eating not only of the green plant, especially at the time of flowering, but also of the grains, straw, stubble, and chaff. It occurs especially in lambs and swine, more rarely in cattle, and very rarely in horses. The symptoms will return even three or four weeks after discontinuance of the food if the animal be exposed to strong sunlight. In the winter the eruption is restricted to a mere itching and burning.

The symptoms consist of a severe erythema of the skin or even a severe dermatitis, and there may be an associated disturbance of respiration, with general symptoms referable to the central nervous system, more particularly if the skin around the head be involved. There seems to be some question as to whether the condition is caused by certain irritant products exerting only a local action on the skin, with secondary general manifestations, or whether it is due to some toxic substance produced in the body of the animal under the influence of sunlight.

Experimental work on laboratory animals, however, seems to show clearly that there is developed some toxic substance in the body of the animal. Ohmke fed rabbits, mice, and guinea-pigs on buckwheat, and death resulted in the white animals exposed to diffused sunlight. The symptoms were loss of hair, paralytic phenomena, and disturbances of respiration. White animals kept in the dark and the gray animals showed no changes.

The chaff as well as the grains gave the same result. Alcoholic extracts of the buckwheat showed a noticeable fluorescence, and proved just as harmful as the buckwheat, while the buckwheat left after extraction was harmless.

Buckwheat poisoning in man seems to have been very rarely noted, and it may be said that we know very little of buckwheat poisoning in the human species.

The relation between the pellagrous erythema and exposure to sunlight has always attracted attention among those interested in this disease, and there seems to be no doubt that some such relation does exist. This relation is, however, not always a very definite one. Pellagrous erythemata are not usual, but, at the same time, are not uncommon on covered parts of the body, and Neusser long ago observed that in the gypsy children of Roumania, who go about naked, the pellagrous erythema is usually confined to local situations—hands, feet, and face. It is worthy of note also that the dark-skinned races suffer from pellagra and from its erythema, and that the negro of the Southern States exhibits erythemas just as extensive and just as severe as those seen in the whites.

If the coloring-matters of corn are of such importance as implied above, then it is likely that the varieties may be a matter of importance. The Italians, in their prophylactic measures, have come to regard the yellow varieties as less likely to undergo spoiling, and they condemn the use of white varieties. White varieties of corn are rarely seen in Italy.

With regard to beriberi and rice, it is interesting to note that Fraser and Stanton, in their experimental work of feeding fowls with rice, state that alcohol-extracted rice

produced the same phenomena as the rice before such extraction, and that rice which has been proved harmless, after being extracted with alcohol, produced typic phenomena in fowls, but that if a quantity of the extract, freed of alcohol, were given at the same time the birds remained well.

Finally, it is to be remarked that the results of feeding experiments upon animals are very difficult of interpretation, and conclusions can be drawn therefrom only with the uttermost caution.

Feeding experiments with maize, made by workers interested in pellagra, have produced many discordant results and varied interpretations. To apply results of this kind to the explanation of a specific disease of man is difficult and uncertain. Such application must be made from wide knowledge, broad experience, and good judgment.

For the purpose of further elucidating these experiments Dr. Lavinder issued a note regarding some experiments gone into by him, and his comments were issued in a bulletin published May 5, 1911. The following is abstracted from his note:

For the purpose of confirming these observations certain experiments were begun February 24th and terminated April 27, 1911.

Cages containing, first, 2 white rabbits and 1 dark one; second, 4 white guinea-pigs and 2 dark ones; third, 6 white mice; and, fourth, 4 white rats, were placed in diffused sunlight, and the animals were fed upon a diet of corn and green food (cabbage, etc.), in approximately a proportion of 4 of the former to 1 of the latter. Control cages on a mixed diet were placed along with the others. All animals

received water freely. An exactly similar series of animals on the same diet were placed in almost absolute darkness.

The corn used in feeding the animals was yellow grain of fairly good quality, and showed no marked evidence of spoiling.

For the first few days it was given uncooked; later, it was cooked into cakes, and this the animals seemed to prefer. It was noticed that unless great care was used in storing it the corn readily became moldy.

Along with the other animals in diffused daylight was placed a cage containing 3 pigeons, 2 dark colored and 1 white spotted. These were fed on an exclusive diet of corn which showed marked evidence of spoiling. They were, of course, given water.

Generally speaking, the results of these experiments were entirely negative. There were several accidental deaths among the animals, but none displayed any such symptomatology as has been described by the writers referred to. All of the animals except the mice did very well on the corn and green food diet, but did not gain as much in weight as did the control animals. A number of the mice died both in the control and in the other cages, but without displaying any characteristic phenomena. They were all young mice, and did not thrive in any of the cages.

The pigeons on spoiled corn were full grown and showed no gain in weight. They remained well.

No differences of consequence were noted between the animals kept in the dark and those exposed to the light.

Dr. John F. Anderson, Director of the Hygienic Laboratory, and Dr. Joseph Goldberger, Past Assistant Surgeon,

have issued a recent bulletin describing an attempt to infect the rhesus monkey with blood and spinal fluid from pellagrins. Their account is given verbatim:

In the literature of pellagra there is not, so far as we are aware, any record of an attempt to infect by inoculation any of the higher animals, such as monkeys, with the blood or tissues from pellagrins.

Sambon's theory of the transmission of pellagra by the buffalo gnat, or *Simulium reptans*, would seem to require that the infecting agent in pellagra be present in the blood at some stage of the disease. From this it follows that, if monkeys are susceptible, the inoculation of blood from cases of the disease should produce pellagra, provided the blood was drawn at a time when the infectious agent was present therein.

During the summer of 1910 we had the opportunity of obtaining some blood from two well-marked cases of pellagra and spinal fluid from one of them. The blood and spinal fluid were used for the inoculation of *Macacus rhesus* monkeys. The details of the experiments are given in the following protocols:

Case 1.—Female, G. M. This patient was a well-marked case of pellagra, showing the acute manifestations of the disease at the time the blood was taken. She was probably in her first attack. Her temperature at the time the blood was drawn was normal.

July 16th, at 11 A. M., about 10 c.c. of blood was drawn from the arm vein, defibrinated, and used as follows:

Cultures were made in fermentation tubes, which remained sterile.

Monkey No. 1, female rhesus. At 12 noon 5 c.c. of the

defibrinated blood from G. M. was inoculated intraperitoneally.

Monkey No. 2, female rhesus. To the fibrin and blood remaining in the flask in which the blood was defibrinated 5 c.c. of normal salt solution was added. The flask was well shaken, 7 c.c. of the fluid drawn off, and inoculated intraperitoneally.

The temperature of both these animals was taken daily until October 21, 1910, when the taking of the temperature was discontinued, but the animals were kept under observation until March 1, 1911.

On August 11, 1911, there was noted an apparent bronzing of the face and a pinkish tint of the neck and upper chest of monkey No. 1. This bronzing and tinting was noted to be more distinct on some days and at times of day than at other times. It persisted for a long time without apparent increase. Nothing unusual was noted with monkey No. 2.

Case 2.—Female, Mrs. G. This patient had a well-marked case of pellagra, with a marked erythema of hands and elbows and a roughened, scaly forehead. The history was unsatisfactory, but the conclusion was reached that she was probably in her second or third attack. When the blood and spinal fluid were taken the patient was in a low muttering delirium and her temperature was between 101.4° and 102.4° F.

On August 24, 1910, at 10:30 A. M. blood was drawn from the arm vein and defibrinated. Cultures were made and found to be sterile. At 10:45 A. M. about 11 c.c. of spinal fluid was withdrawn. Cultures were made in fermentation tubes and found to be sterile.

Monkey No. 3, female rhesus. At 12:10 P. M. inoculated with 6 c.c. of the defibrinated blood intraperitoneally.

Monkey No. 4, male rhesus. At 12:05 P. M. inoculated with 6 c.c. of the defibrinated blood intraperitoneally.

Monkey No. 5, female rhesus. At 11:55 A. M. inoculated with 10 c.c. of the spinal fluid intraperitoneally.

Daily temperatures were taken of all three of the monkeys until October 21, 1910, when the taking of temperatures were discontinued. The observations, however, were continued until about March 1, 1911.

None of the monkeys presented anything worthy of note, except that it was thought, about September 15th, that monkey No. 3 showed a slight reddening of the skin in the region of the eyebrows. This, however, lasted only a few days.

During the entire time the monkeys were kept under observation they were in a well-lighted room and exposed to a certain amount of sunlight on bright days. Their food was that given to other monkeys in the laboratory, it not being considered advisable to make any change in their diet, as the question it was wished to determine by the inoculation of the fluids from the cases of pellagra was as to whether the blood or the spinal fluid from such cases, when inoculated into monkeys, was able to produce pellagra in these animals.

Summary.—The blood from 2 cases of pellagra and the spinal fluid from one of them were not infective for the rhesus monkeys.

Interpretation.—The foregoing results permits of several interpretations. Thus it may be (1) that the rhesus monkey is not susceptible to pellagra; or (2) if susceptible,

(a) that our technic in some respects was faulty, or (b) that, while the technic was adequate, the infective agent was not present in the blood or in the spinal fluid at this stage of the disease.

Extending this last interpretation, one may suspect that the infective agent in pellagra never resides in the blood or spinal fluid. *A final conclusion, however, is not justified.*

The writer of this book regrets that the agent etiologically responsible for pellagra has not been found beyond a per-adventure.

From the army of earnest students now in quest of this etiologic agent much may be expected, and, while we are zealously endeavoring to cope with the situation as it confronts us in this country, especially in the South, we look forward to a good day in the not-too-distant future when doubt will give way to certainty, and hypothesis will become assured fact, Gibraltar-like in its foundation.

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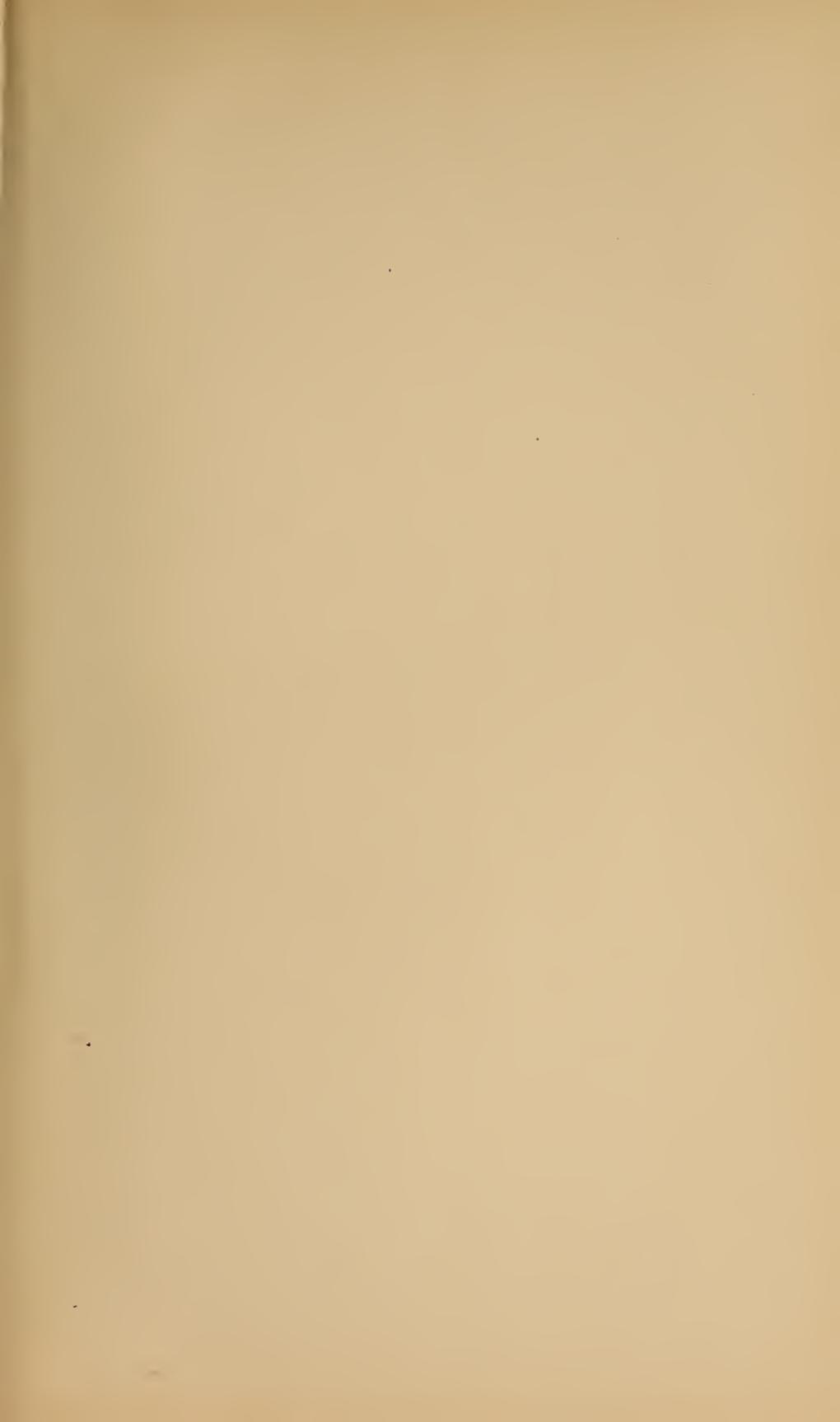
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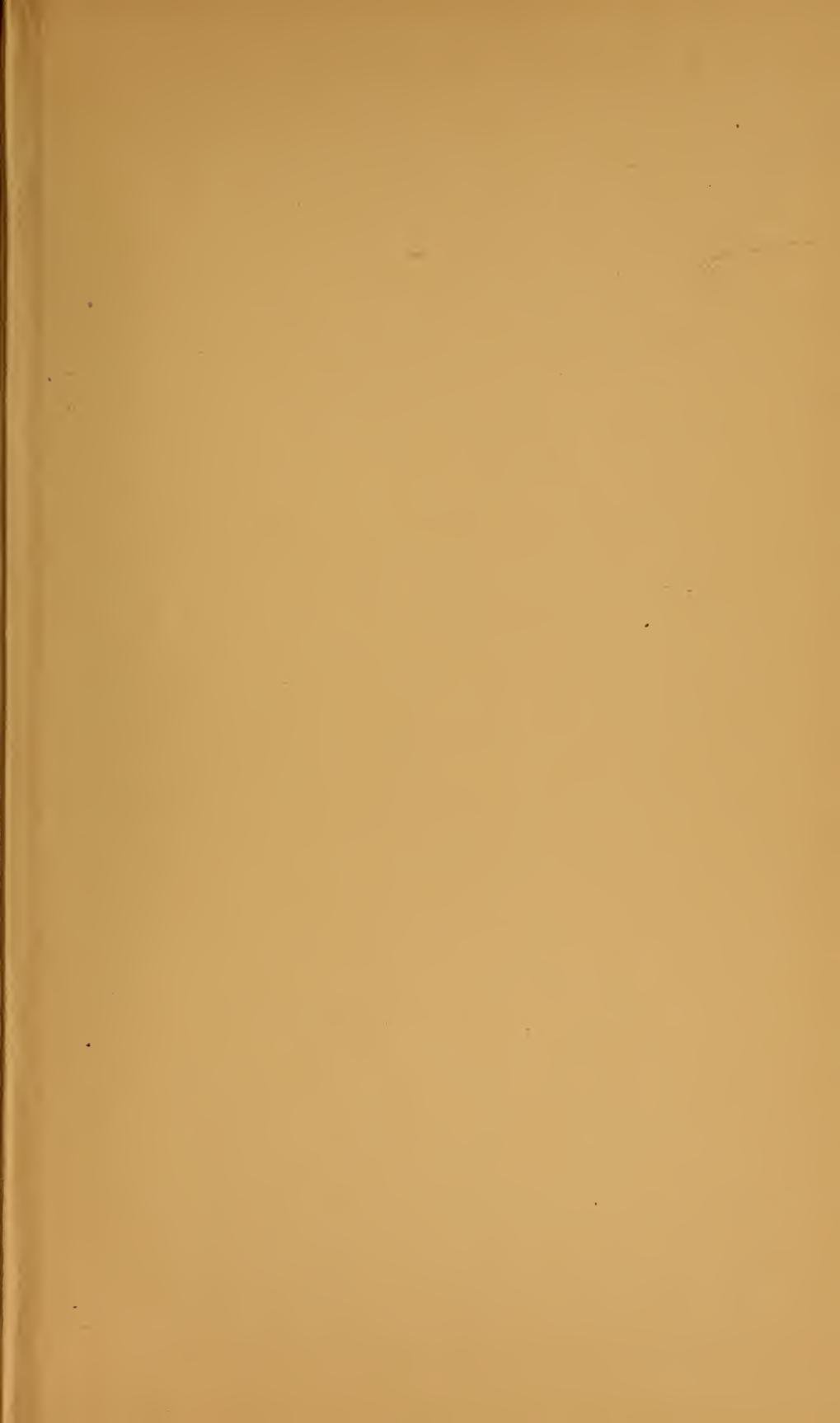
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